TRANSACTIONS

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of
OPHTHALMOLOGY
and
OTOLARYNGOLOGY

JANUARY - FEBRUARY
1956

Volume 60 Number 1

ANNUAL MEETING, OCTOBER 14-19, 1956, CHICAGO

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TRANSACTIONS

American Academy of Ophthalmology and Otolaryngology

VOLUME 60 JANUARY - FEBRUARY, 1956 NUMBER 1

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inflammatory, allergic eye disorders

prompt relief

in acute episodes

continuing benefits

when needed

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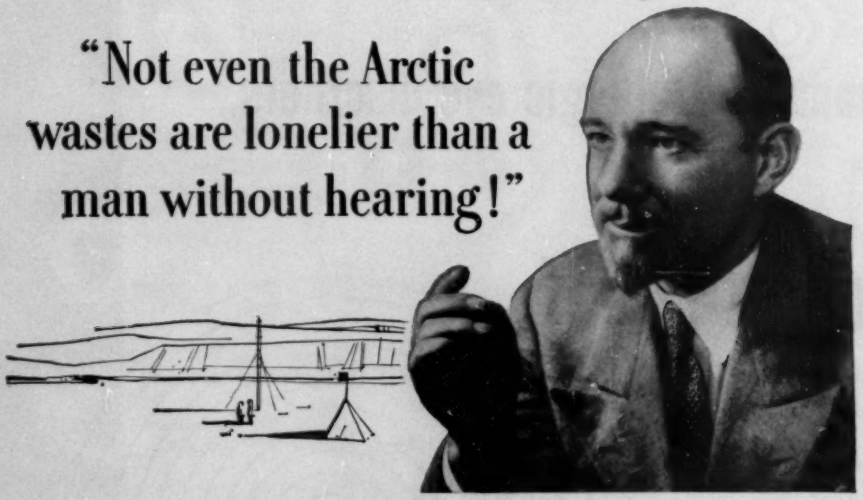

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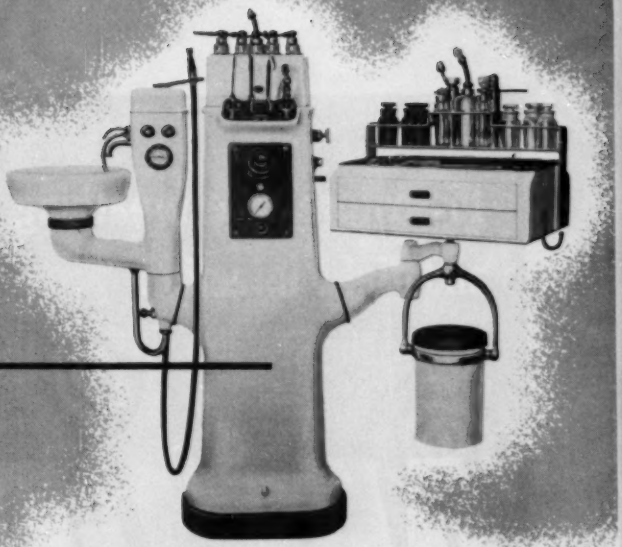

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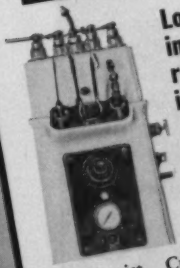

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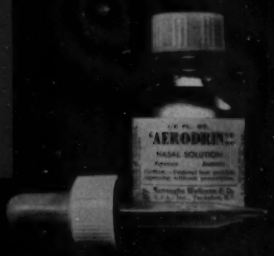

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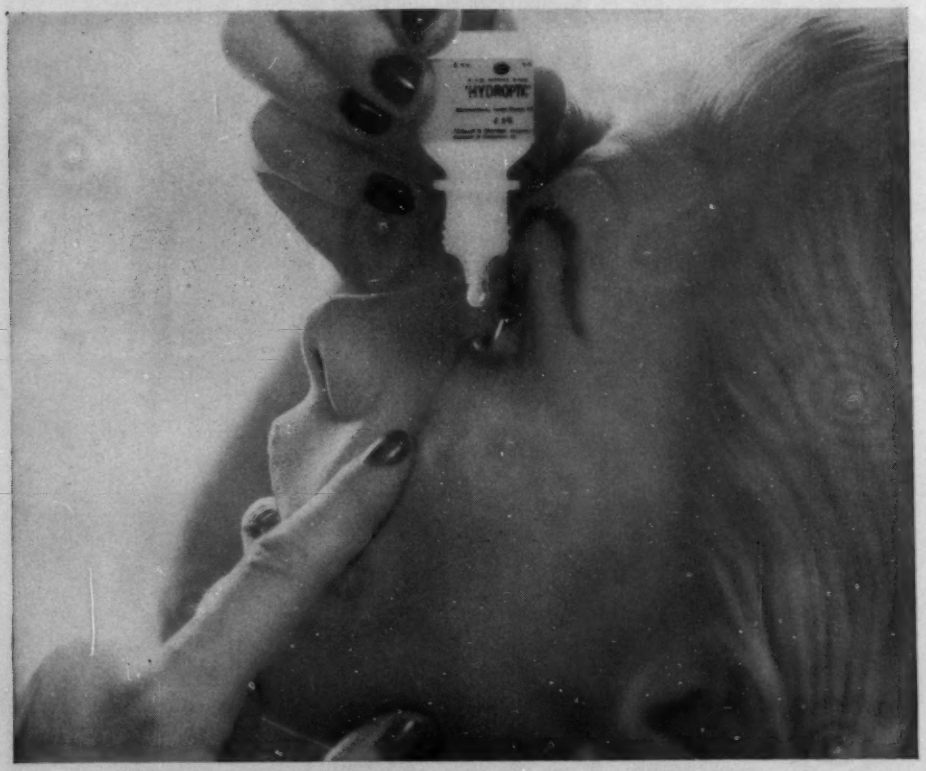

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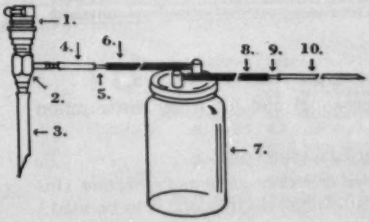

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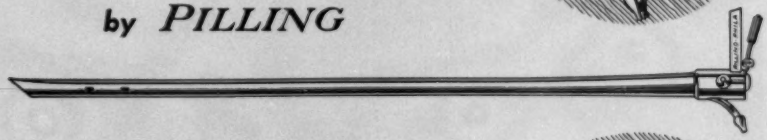

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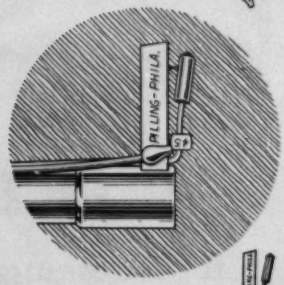

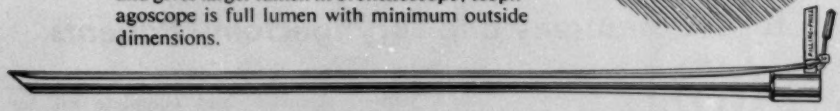

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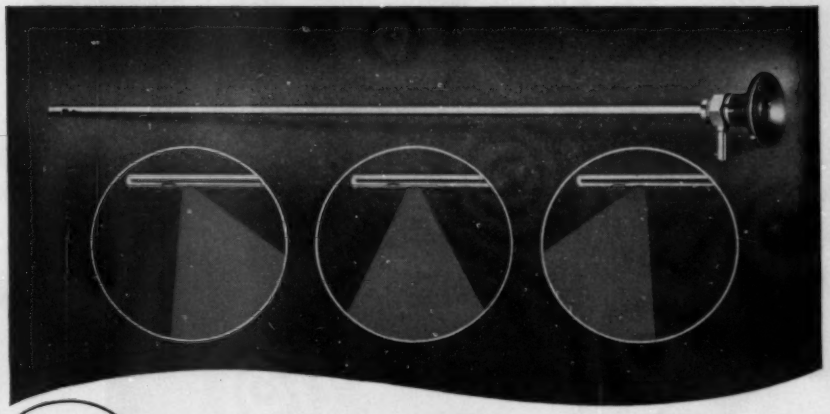

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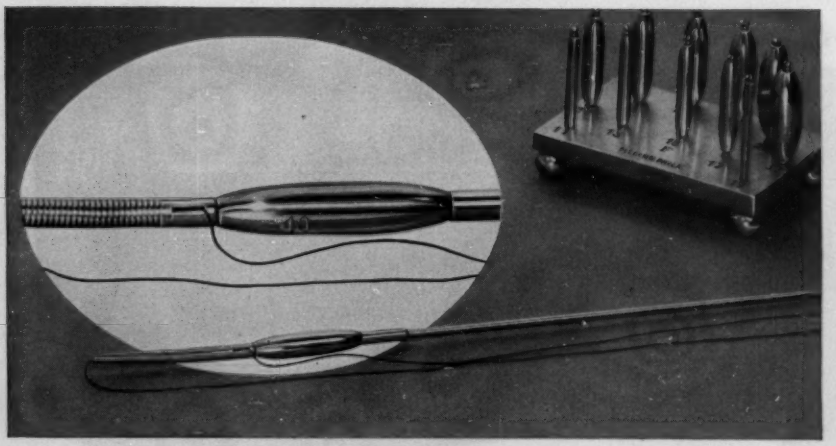

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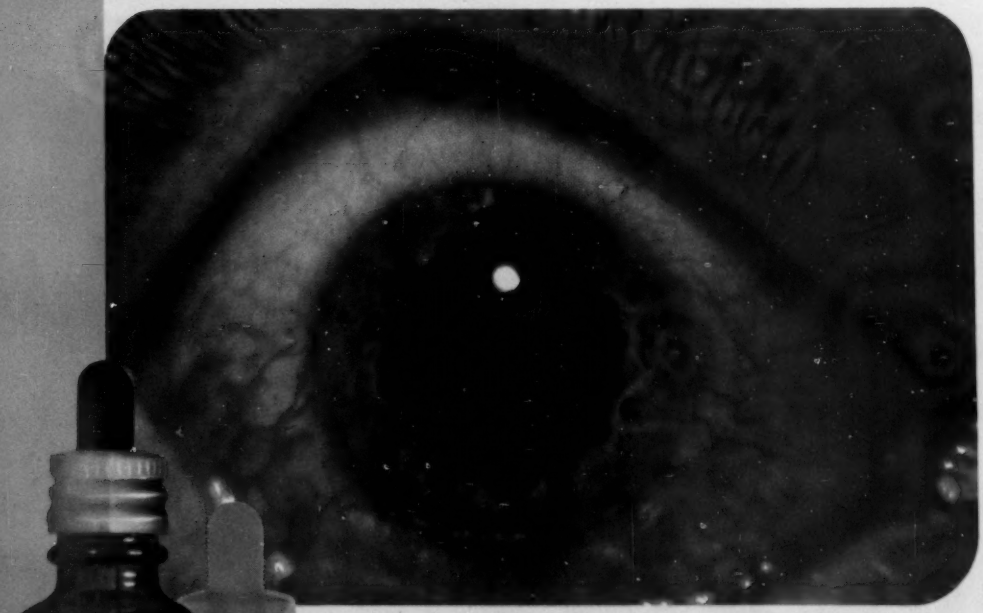

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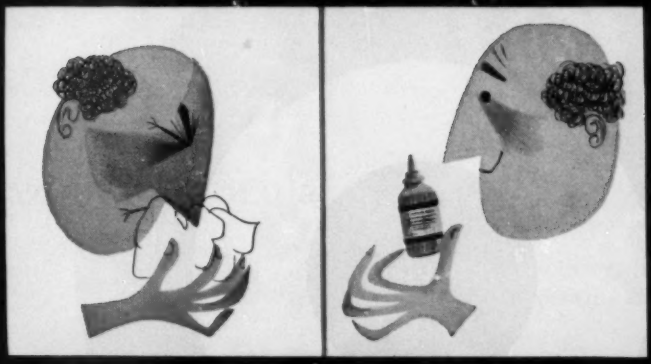

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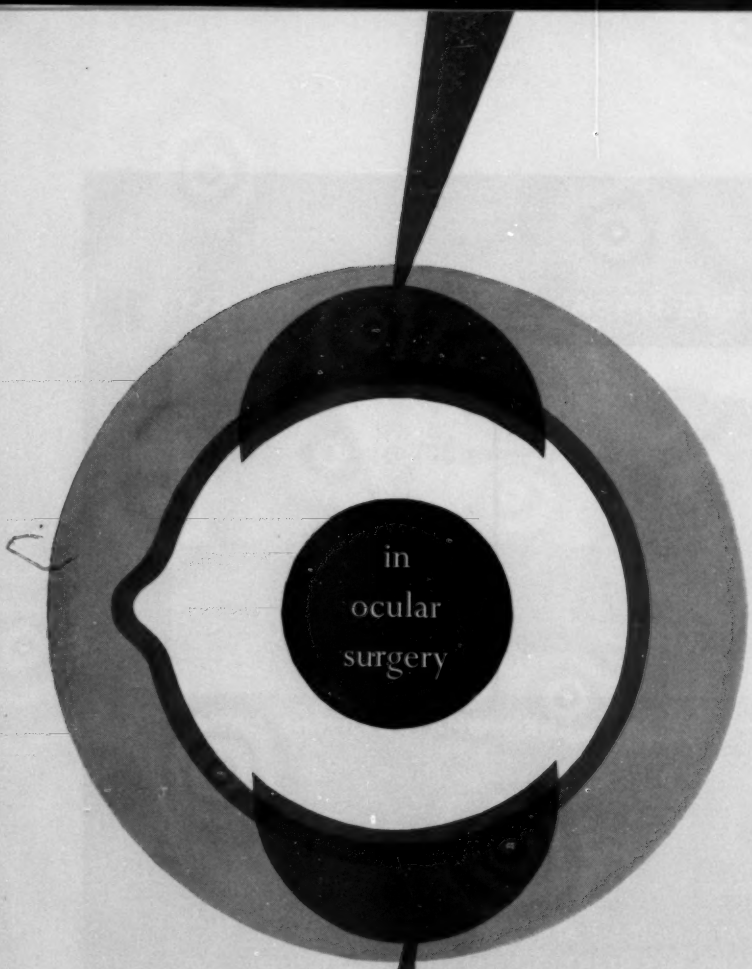

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–Nutt and Wilson[4]

1. Am. J. Ophth. *38*:576 (Oct.) 1954.
2. Brit. J. Ophth. *39*:109 (Feb.) 1955.
3. Canad. Anaesth. Soc. J. *2*:191 (Apr.) 1955.
4. Brit. M. J. *1*:1457 (June 18) 1955.

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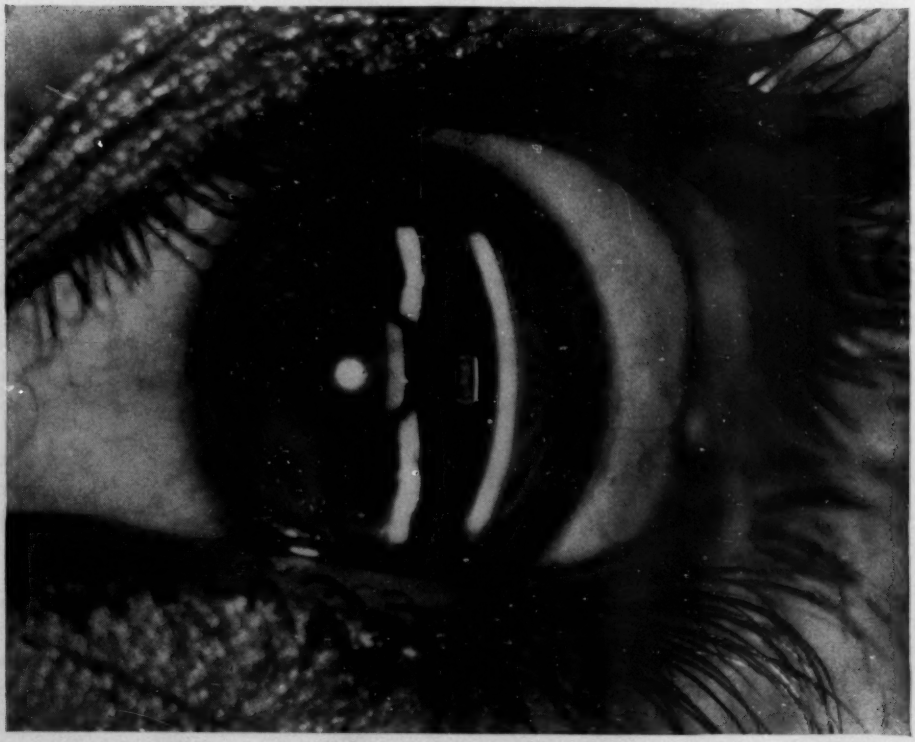
topical
sight savers



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Reference: 1. Hogan, M. J., Thygeson, P. and Kimuras, J., *Arch. Ophth.* 53:165, Feb. 1955.

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A Laboratory and Clinical Report on Adrenosem® Salicylate

(BRAND OF CARBAZOCHROME SALICYLATE)

History

The first investigation of a hemostat with an action comparable to Adrenosem Salicylate was made by Derouaux and Roskam[1] in 1937. They reported that an oxidation product of adrenalin, adrenochrome (which has no sympathomimetic properties), has prompt hemostatic activity.

It was further found that various combinations of adrenochrome, notably the oxime and semicarbazone, produced stable solutions. But, these were so slightly soluble that sufficient concentration could not be obtained for practical therapeutic use. By combining these adrenochrome compounds in a sodium salicylate complex a stable, soluble form can be obtained. This complex has been given the generic name, carbazochrome salicylate, and is supplied under the trade name Adrenosem Salicylate.

Roskam, in his study entitled "The Arrest of Bleeding,"[2] enumerates "the drugs whose efficaciousness as hemostatics have been proved by accurate methods in experimental animals and in healthy men as well. . . . One is the monosemicarbazone of adrenochrome [Adrenosem Salicylate]."

Chemistry

Adrenosem Salicylate is a synthetic chemical. The full chemical name is adrenochrome monosemicarbazone sodium salicylate complex.

Pharmacology

Although it is chemically related to epinephrine, Adrenosem Salicylate has no sympathomimetic effects. It does not alter blood components, nor does it affect blood pressure or cardiac rate.[2-7]

(* U.S. Patent 2,581,850)

Sherber, in an early study,[3] concludes that Adrenosem Salicylate* "is a potent antihemorrhagic factor in those conditions in which the integrity of the smaller vessels is interrupted, and is superior to any similar material that is now available."

He continues, "From our experience it appears that adrenochromazone complex is indicated in preventing vascular accidents incident to hypertension; in maintaining small vessel integrity; in the preoperative preparation where oozing from a vascular bed is anticipated, as in tonsillectomies, adenoidectomies and prostatectomies; and as an adjunct in the treatment of bleeding from such surgical procedures."

Adrenosem Salicylate may be administered simultaneously (but separately) with any type of anesthetic, anticoagulant, or vitamin K and heparin.

A Unique Systemic Hemostat

Clinical investigators[2-7] are in agreement that Adrenosem Salicylate controls bleeding and oozing by decreasing capillary permeability and by promoting the retraction of severed capillary ends. It aids in maintaining normal capillary integrity by direct action on the intercellular "cement" in capillary walls. The interesting work of Fulton[8] confirms this. Adrenosem Salicylate, since it is not a vasoconstrictor, has no effect on large severed blood vessels and arterioles.

Adrenosem Salicylate is being used both prophylactically and therapeutically in thousands of hospitals, and in virtually every type of surgical procedure. It has also proved most useful in dental surgery.[7]

Owings reported on the use of Adrenosem Salicylate in controlling postoperative adenoid bleeding in 102 cases.[4] "We have used 2½ mg.

(½ ampule) intramuscularly, 15 minutes before anesthesia for children and 5 mg. (1 ampule) for adults." In only one patient did bleeding occur. Three others showed red blood from the nose and mouth. These patients "were then given 5 mg. intramuscularly, with prompt and complete control. We have also noticed that bleeding stopped more promptly on the operating table."

This is a 1% incidence of postoperative bleeding using Adrenosem Salicylate preoperatively, compared to an incidence of 10% postoperative bleeding in all cases taken from previous records, without Adrenosem Salicylate medication.

Peele reports on the use of Adrenosem Salicylate in treating 178 patients with 24 different conditions.[5] The drug was first used to control postoperative hemorrhage from the adenoid region. He adds: "The results were so dramatic that since that date [1953] Adrenosem Salicylate has been used postoperatively to reduce bleeding from all otolaryngologic and bronchoesophagolic procedures, to treat postoperative hemorrhage from the tonsil and adenoid regions, and to treat selected cases of epistaxis."

The effectiveness of Adrenosem Salicylate in controlling bleeding and oozing in 330 patients is reviewed by Bacala.[6] "Our experience of the effect of carbazochrome salicylate on 317 surgical indications and 13 obstetricogynecological conditions, has been therapeutically encouraging and successful for the control of capillary bleeding. Foremost among the cases studied were 223 tonsillectomies definitely benefited by this metabolic hemostat, making a diminution of the control incidence of posttonsillectomy bleeding of 19.8% down to 7%. It has also been found useful in gastro-intestinal bleeding, cataract extraction, epistaxis, incisional seepage, trans-urethral prostatectomy, menometrorrhagias, cervical ooze, antepartum and postpartum bleeding, threatened abortion, and prevention of capillary hemorrhages during hedulin or dicumerol therapy."

Side Effects

All investigators concur that, at recommended dosage levels, Adrenosem Salicylate is free from toxic effects. No cumulative effects attributable to the drug have been reported.

The only side reaction noted has been a transient stinging sensation in the area of injection when Adrenosem Salicylate is used intramuscularly. As one investigator comments: "The brief discomfort which attends the injection of Adrenosem into the gluteal region has not been a significant problem in children or adults as originally anticipated."[5]

Indications

Idiopathic purpura, retinal hemorrhage, familial telangiectasia, epistaxis, hemoptysis, hematuria.

Postoperative bleeding associated with:
tonsillectomy, adenoidectomy and
nasopharynx surgery;
prostatic and bladder surgery;
uterine bleeding;
postpartum hemorrhage;
dental surgery;
chest surgery and chronic pulmonary bleeding.

Dosage

For recommended dosage schedules, please send for detailed literature.

Supplied

Ampuls: 5 mg., 1 cc. (package of 5).
Tablets: 1 mg. S.C. Orange, bottles of 50.
Tablets: 2.5 mg. S.C. Yellow, bottles of 50.
Syrup: 2.5 mg. per 5 cc. (1 tsp.), 4 ounce bottles.

References

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3. Sherber, Daniel A.: The Control of Bleeding, Am. J. Surg. **86**:331 (1953).
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5. Peele, J.C.: Adrenosem in the Control of Hemorrhage from the Nose and Throat, A.M.A. Arch. of Otolaryng. **61**:450 (April, 1955).
6. Bacala, J.C.: The Use of the Metabolic Hemostat, Adrenosem Salicylate. To be published.
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8. Fulton, M.D., Dept. of Biology, Boston University: Personal Communication.

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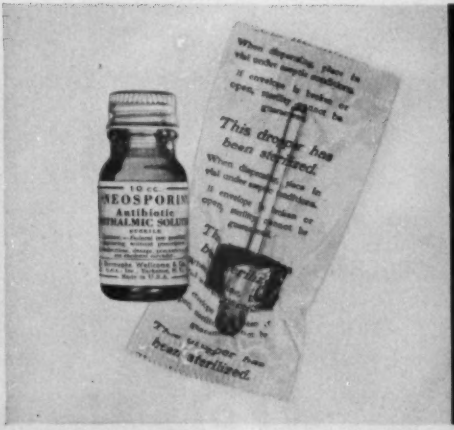

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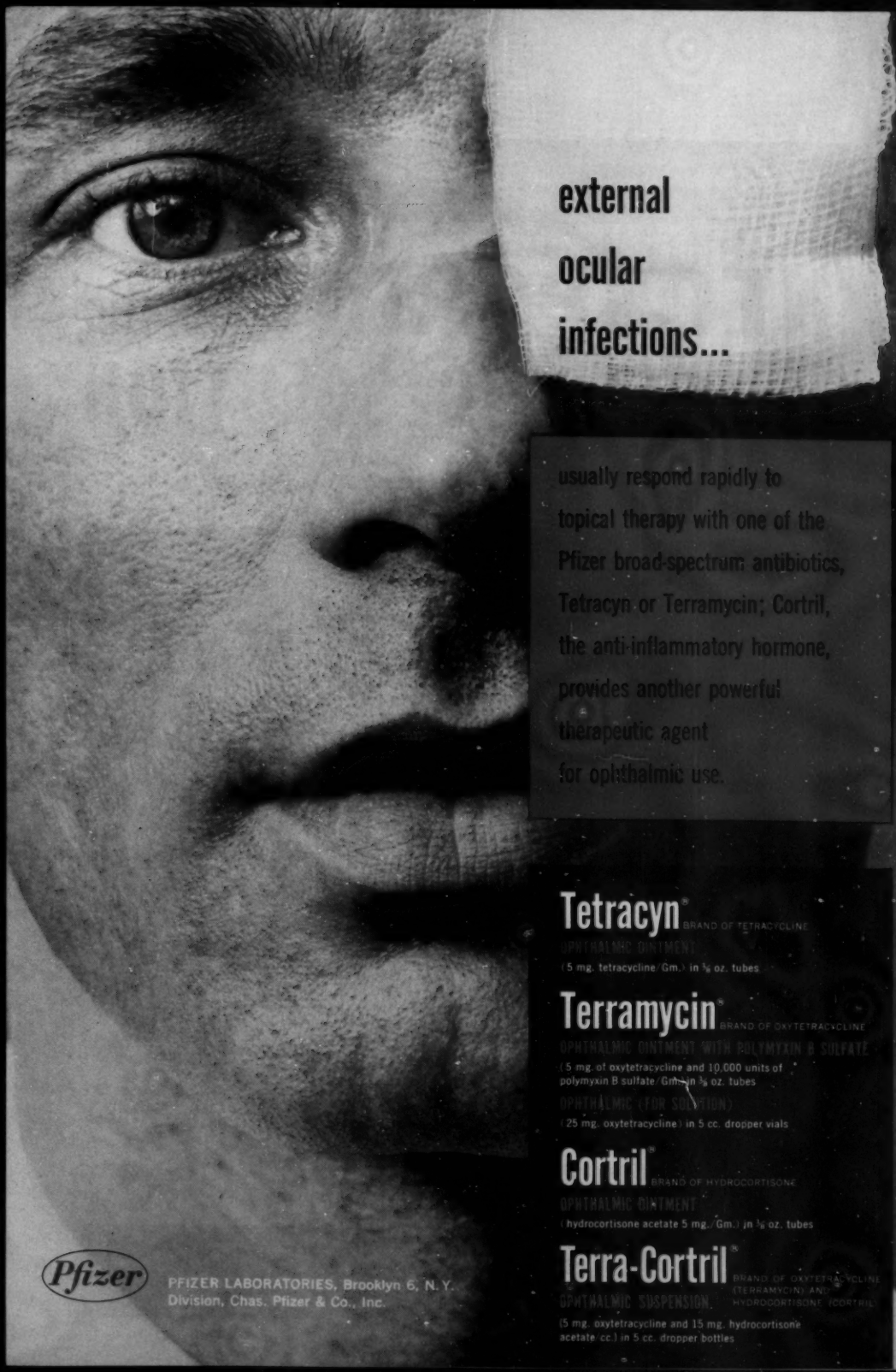
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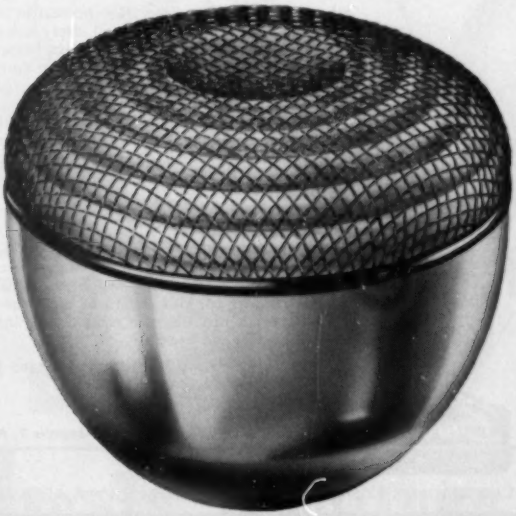

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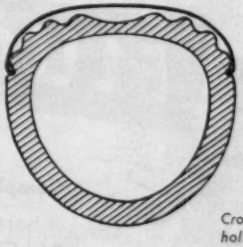

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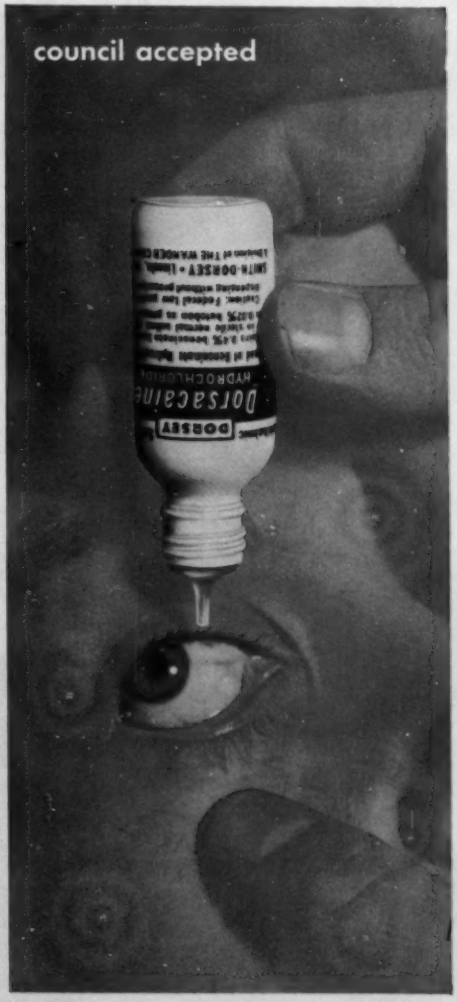

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*Schlegel, H. E., Jr., and Swan, K. C.: A. M. A. Arch. Ophth. *51*:863 (May) 1954.

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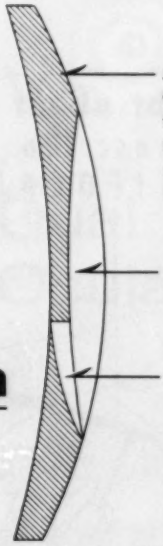
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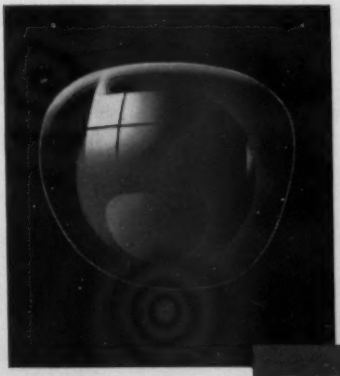

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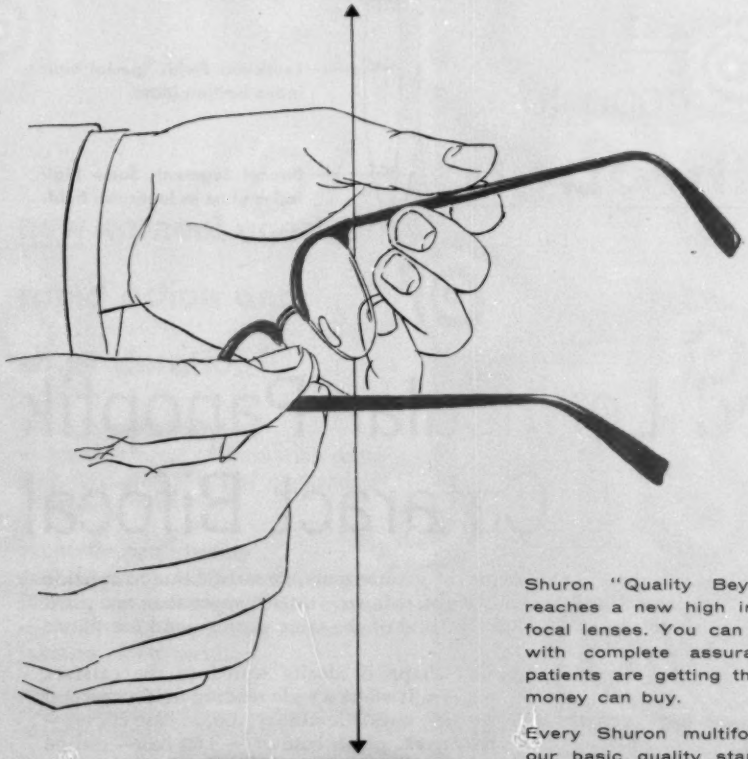

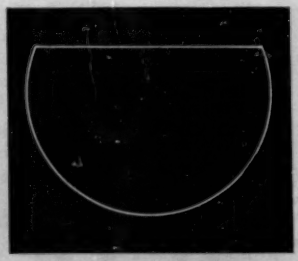

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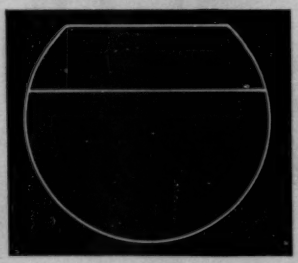

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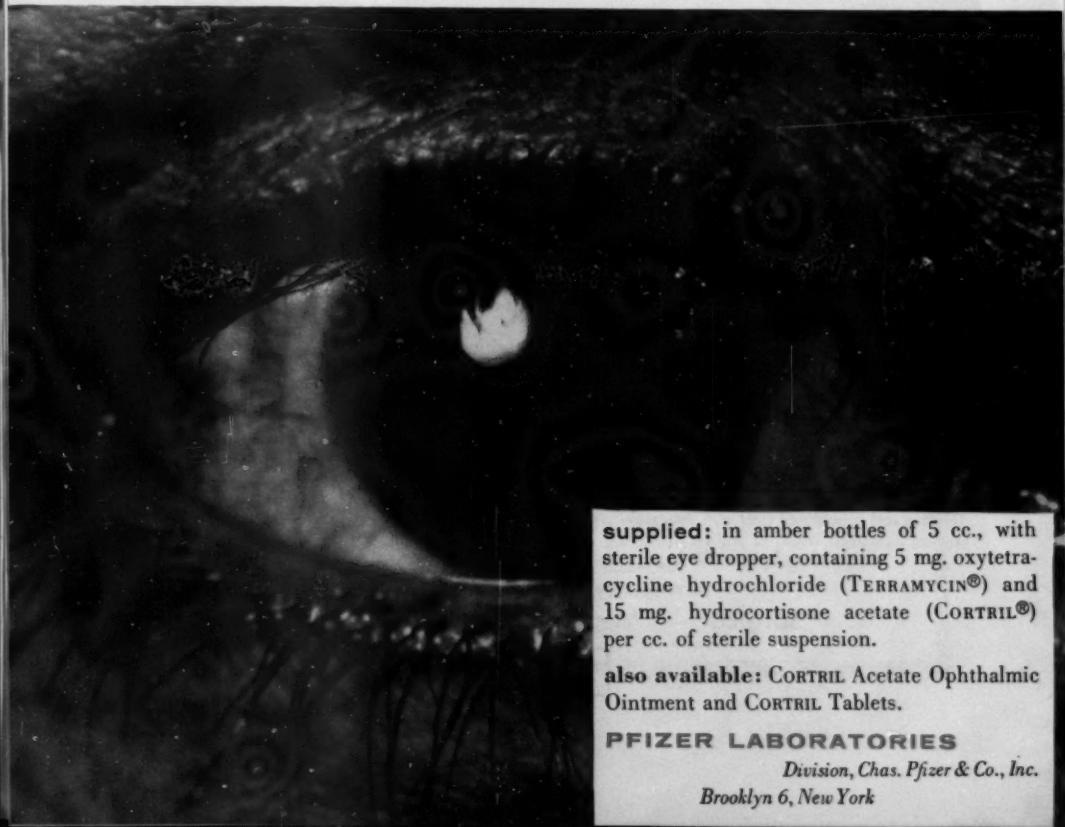

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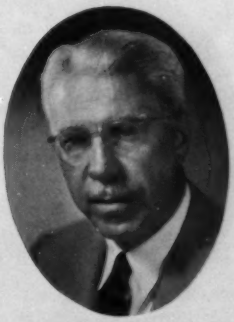

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A sound understanding of optic nerve disease must be based on a knowledge of (1) anatomy and physiology, (2) pathology, and (3) visual field changes.

From the Department of Ophthalmology, College of Physicians and Surgeons, Columbia University, and the Institute of Ophthalmology, Presbyterian Hospital, New York.

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Presented at the Sixtieth Annual Session of the American Academy of Ophthalmology and Otolaryngology, October 9-14, 1955, Chicago.

I

ANATOMY AND PHYSIOLOGY; SYMPTOMS AND SIGNS

JOHN WOODWORTH HENDERSON, M.D.
ANN ARBOR, MICHIGAN

THE optic nerve is not a true peripheral nerve; it is, rather, a fiber tract of the central nervous system. Embryologically, its fibers are derived from the retina, an outpouching of the primitive forebrain, and grow through the connecting optic stalk to reach their central connections. The optic nerve transmits a sensory stimulus to the thalamus for relay to the cortex and is comparable to the ascending sensory fiber tracts of the spinal cord and brain stem. Like them, its fibers have no neurilemmal sheath; it lacks the specialized connective tissue framework of cerebrospinal nerves, and it possesses the characteristic glial framework of other white matter of the cerebrospinal axis.

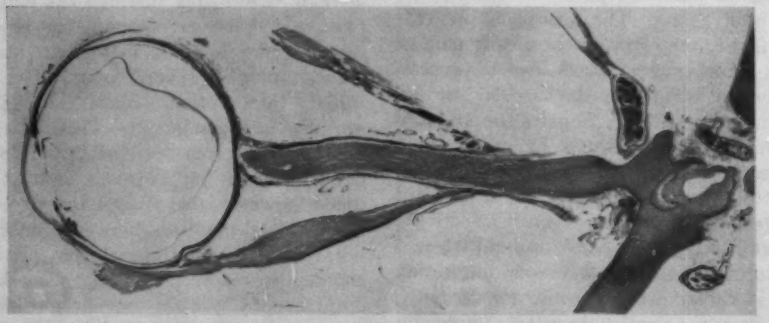


Fig. 1—Anatomy of the optic nerve. (Courtesy of Armed Forces Institute of Pathology.)

In its total course from globe to optic chiasm, the nerve is about 5 cm. in length (fig. 1), and may be subdivided into four portions: intracranial, intracanalicular, intraorbital, and intraocular. The intracranial part varies in length with chiasmal position, but averages 10 mm.; the intracanalicular portion is about 6 mm. in length; the intraorbital section averages 30 mm.; and the intraocular part measures 0.7 mm.

The posterior scleral foramen of the globe contains the intraocular portion of the nerve. Here the nerve fiber layer of the retina converges from the periphery to a common exit at the papilla. The nerve thus formed is narrow at the foramen because of lack of myelin sheaths, but as it emerges through the lamina cribrosa, myelin is added and the nerve becomes wider. In the papilla, anterior to the lamina cribrosa, there are no fibers of Müller as in the surrounding retina, perhaps one reason why the disc may swell readily while the surrounding retina remains relatively flat.

The intraorbital portion of the nerve emerges from the globe just above and somewhat nasal to the posterior pole and

courses in an upward and inward direction to reach the optic foramen at the apex of the orbit. Since the nerve averages 30 mm. in length, and the distance from the globe to foramen averages only 18 mm., a sinuous course allows for freedom of ocular movement, and permits considerable proptosis before traction effects will occur. Surrounded by the muscle cone, by motor, sensory and autonomic nerve branches, all embedded in orbital fat, the optic nerve passes backward through the annulus of Zinn before entering the optic canal.

Through its intraorbital course, the optic nerve is covered by sheaths which are continuous with those of the brain. The dural sheath of the nerve is continuous with the inner layer of the cranial dura. Beneath the dural sheath of the optic nerve is a capillary layer—the subdural space. The subjacent arachnoid layer is continuous with the intracranial arachnoid and forms the outer boundary of the subarachnoid space. The inner limit of this space is the pial layer, which carries vessels and dividing septa into the nerve proper. Anteriorly, all three meningeal layers and the enclosed spaces end at the globe, with no definite intraocular communication. Posteriorly, the subarachnoid space of the nerve sheath communicates through the optic foramen with the corresponding intracranial space, but the subdural space probably has no direct communication.

At the optic foramen the nerve sheath is closely adherent to the origin of the superior and medial rectus muscles. Thus movement or palpation of the eyeball in cases of optic neuritis may give rise to pain or tenderness, probably from irritation to the trigeminal nerve endings in the involved sheath about the optic nerve.

Within the optic canal the dura is bound firmly to the optic nerve. Only below is there a looser subarachnoid space communicating through to the cranial fossa. This limited aperture can be readily closed by pressure from above within the cranial cavity and explains the occurrence of optic atrophy rather than papilledema in certain frontal lobe tumors. Such a firm fixation within the canal also prevents a shift of the nerve through the foramen under conditions of trauma.

Accompanied by the ophthalmic artery lying below within the dural sheath, the intracanalicular optic nerve lies in relation medially with the sphenoid sinus or a posterior ethmoid air cell, usually separated by only a thin sheet of bone. In some cases, however, a bony dehiscence will allow direct contiguity of nerve sheath and sinus mucosa. This close relationship has been cited to explain the causation of retrobulbar neuritis by sinus disease.

The intracranial segment of the optic nerve lies in close relationship to many vital structures. Its length and relations vary with chiasmal position. Beneath it are the diaphragma sellae of the pituitary gland and the cavernous sinus with its enclosed sensory and motor nerves. Farther forward, the internal carotid artery gives off the ophthalmic branch beneath the nerve. Above lie the anterior perforated substance, the olfactory tract, and the anterior cerebral artery. Laterally, the internal carotid artery bifurcates into the anterior and middle cerebral branches.

The blood supply of the optic nerve is furnished by a fine network of pial vessels which enter the periphery of the nerve to form the dividing septa (fig. 2). The thickness of each septum is proportional to the size of the contained vessel, and the nerve fibers are divided into fascicles by the septal system.

All divisions of the nerve except the intracranial portion are supplied by branches of the ophthalmic artery. The

FIG. 2—Pial septums of the optic nerve showing contained blood vessels. (H & E; × 75) (Courtesy of Armed Forces Institute of Pathology.)

intraocular portion of the nerve is fed by branches of the arterial circle of Zinn, as well as by branches of the central retinal artery. Recent injection experiments[8] show a free anastomosis between these two vascular supplies in the region of the lamina cribrosa.

The arteries which supply the pial sheath network posterior to the central vessel entrance into the nerve are derived from branches of the ophthalmic artery. These are from six to twelve in number and pierce the dura to join the pial network. In general, they enter above and on the sides, since the under portion is supplied by recurrent branches from those farther forward.[7]

The orbital portion of the optic nerve appears to have a dual arterial supply. The outer pial network penetrates the periphery of the nerve, and a system of axial vessels supplies the core of the nerve. Whether anastomoses exist between these two systems is still in doubt.

The source and composition of the axial vessels have been studied by many workers. The varying opinions have been reviewed recently, and the anatomy investigated by injection methods (fig. 3).[4] Earlier it was thought that a central system was present, with no contribution from the central retinal artery once it enters the sheath.[1,6] A discontinuous axial supply, also independent of the central retinal artery, was described in a later article.[2] Another worker found that a well-defined axial artery arises from the central retinal artery as it enters the nerve sheath.[7] Most recently,[4] by means of injection methods, it has been shown that the central retinal artery is entirely independent of both the optic nerve and the anastomotic connections of the circle of Zinn—supplying the retina exclusively. An independent axial vessel, termed the central optic nerve artery, arises from the ophthalmic artery early in its course and enters the nerve independent of the central retinal artery. Within the nerve this axial vessel courses forward to anastomose with the arterial circle of Zinn and backward as far as the optic foramen. It was concluded that the central optic nerve artery is designed to feed the macular fibers and to act also as vasa vasorum for the central retinal artery itself.

It should be noted that since variability of vascular supply is often the rule in other bodily locations, incompatability of the views just given may express a normal variation.

In contrast to such a limited supply for the papillomacular bundle, it should be emphasized that the outer pial network of the optic nerve has a rich arterial circulation by way of the ophthalmic artery, with collateral circula-

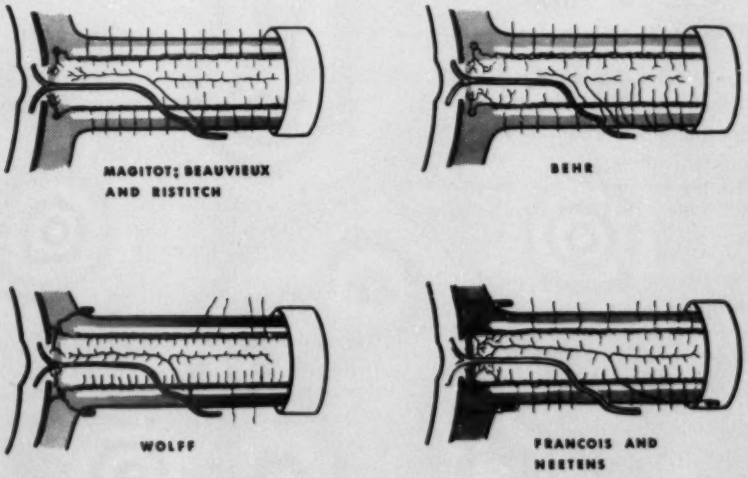
tion from many internal and external carotid branches, including the anastomosis between the lacrimal and middle meningeal arteries.[4]

Whether the axial system continues into the intracanalicular and intracranial optic nerve is not yet certain. One authority states that the intracanalicular part of the nerve is supplied by the ophthalmic artery, but that the pial network is poorer.[7] Many and various adjacent branches supply the chiasm and the intracranial optic nerve.

It seems reasonable to infer that involvement or sparing of the papillomacular bundle in various disease entities may possibly be related to the peculiarities of the blood supply.

area, the papillomacular bundle occupies the temporal third of the nerve head and remains in this position in the nerve as it emerges from the globe. It gradually moves to the core of the nerve in its course toward the optic foramen; just as it enters the chiasm, it is found in the exact center of the nerve. In this course the fibers from the retinal quadrants remain in the same relationship to each other as in the retinal areas represented.

The mode and site of passage of the central retinal vessels across the sheaths of the optic nerve may have important clinical implications. It has been shown that the central retinal artery crosses directly through the vaginal space to



ARTERIAL SUPPLY OF OPTIC NERVE

FIG. 3—The arterial supply of the optic nerve (redrawn from Francois and Neetens).

Since many patients with optic neuritis exhibit a central scotoma, the fibers from the macula are very important in a discussion of disease of the optic nerve. Carrying impulses from the macular

enter the nerve but the vein has a variable course (fig. 4).[5] In about half the cases, the central retinal vein also crosses directly, but in the others, the intravaginal course is more prolonged. This exposes

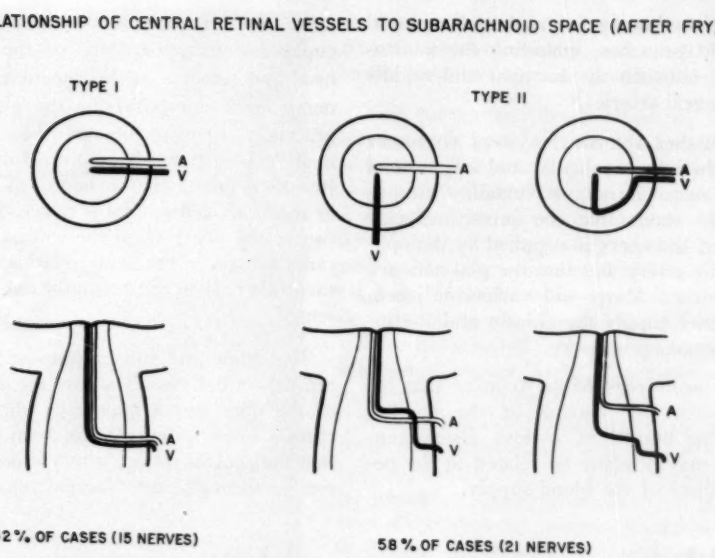

RELATIONSHIP OF CENTRAL RETINAL VESSELS TO SUBARACHNOID SPACE (AFTER FRY)
TYPE I
TYPE II
A
V
42 % OF CASES (15 NERVES)
58 % OF CASES (21 NERVES)

FIG. 4—Anatomical variation in the course of the central retinal vein (redrawn from Fry).

the relatively distensible vein to compression from the increased cerebrospinal fluid pressure in the subarachnoid space and is thought to be a major factor in the production of papilledema associated with increased intracranial pressure.

The site of the lesion in relationship to the point of entrance of the central retinal vessels into the optic nerve probably determines whether or not early visible swelling will occur in the optic disc. Lesions distal to such entrance are said to produce swelling in the optic nerve head, while those behind this point produce no recognizable fundus changes in their acute phase.

The optic nerve contains visual fibers, pupillomotor fibers, and efferent fibers which are thought to be vasomotor in function. Whether the pupillomotor fibers are distinct from the visual fibers has not been determined. The optic nerve behaves like other sensory nerves and conducts visual stimuli in one direction —toward the primary optic centers. The adequate stimulus consists of impulses generated in the receptor organs of the retina. Each nerve fiber acts according to the all-or-none principle, and the presence of oxygen is necessary, so that interference with the circulation results in an immediate block of impulses.

Localized pressure on the optic nerve will produce a "physiologic block" of conduction. Some instances of such blindness may recover immediately with removal of the tumor. Long continued pressure may lead to degeneration by progressive interference with the blood supply.

Recent work has shown that a block of nerve conduction can be produced by the retrobulbar injection of procaine.[3] In general, peripheral field loss occurred first, suggesting absorption by way of the outer pial network. The authors believe that the visual impairment of papillitis or retrobulbar neuritis is a sensory nerve block stemming from the disease process.

The clinical findings in optic neuritis as based on the anatomy follow:

1. Visual loss
2. Visual field defect
3. Pain in or behind the eye on ocular movement or by palpation of the globe
4. Decreased pupillary light reaction
5. Ophthalmoscopic changes

The loss of vision varies with the location of the lesion in the nerve, but it is usually due to a defect in central vision related to the visual field finding of a negative central or centrocecal scotoma. This is based on involvement of the papillomacular bundle. However, any type of field defect is possible.

Ocular or orbital discomfort may be a presenting symptom. Pain on movement of the eye or on palpation of the globe (which occurs in 20 per cent of cases) is thought to be due to traction on the inflamed nerve sheath by the rectus muscles.

The diminished direct pupillary light reaction present in some cases is what would be expected with a conduction block.

Ophthalmoscopic evidence of acute optic neuritis occurs only when involvement is near the globe. In early retrobulbar neuritis, the nerve head appears unchanged. Later, pallor may be seen regardless of the original location of the lesion.

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II

HISTOLOGY AND GENERAL PATHOLOGY OF THE OPTIC NERVE

LORENZ E. ZIMMERMAN, M.D.
WASHINGTON, D. C.
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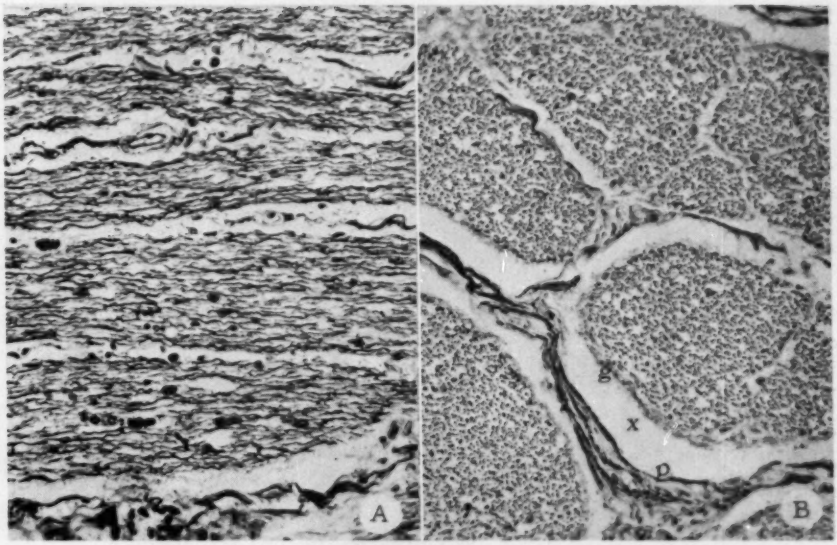

FIG. 1—AFIP Acc. 114419. Axis cylinders of normal optic nerve demonstrated by Bodian's method. (A) Longitudinal section, × 265. (B) Cross section, × 265. The clear unstained zone about each axis cylinder represents the lipoidal myelin sheath. The broad clear space (x) about each bundle of nerve fibers is an artefact resulting from shrinkage during fixation. Actually the glial limiting membrane (g) should be in apposition with the pial septum (p). See figure 4,A for hematoxylin-eosin stained section of same optic nerve.

HISTOLOGY

THE relatively simple structure of the optic nerve may be described in terms of its essential components. These are (1) the partially myelinated nerve fibers; (2) the interstitial cells, which include (a) oligodendrocytes, (b) astrocytes, and (c) microglia; and (3) the fibrovascular septums of pia mater which subdivide the nerve into bundles of nerve fibers.

The nerve fiber has two principal components, an axis cylinder and a myelin sheath. The axis cylinder is the very long, fine protoplasmic extension from the ganglion cell located in the retina to the lateral geniculate body. Posterior to the lamina cribrosa it acquires a sheath of myelin. As seen in cross section, the

From the Veterans Administration Central Laboratory for Anatomical Pathology, Armed Forces Institute of Pathology.

FIG. 2—Normal glia of optic nerve demonstrated by silver carbonate impregnation. (A) An astrocyte with long fibrous processes occupies the center of the field. (B) Another fibrous astrocyte. The small cells arranged in columns in (A) and (B) are oligodendrocytes. (C) These astrocytic fibers form the intrinsic framework of the optic nerve. The very faintly stained fibers passing vertically are the axis cylinders which are not stained well by this technique. (D) The small cell with irregular dendritic processes in the center of the field is a microglia. The other nuclei are those of oligodendroglia. (We are indebted to Dr. J. Reimer Wolter, Neuropathology Laboratory, University of Michigan, for permission to use these magnificent preparations which he made and photographed.)

axon is a small dark-staining dot surrounded by a clear halo (fig. 1), which represents the myelin sheath.

There are three types of supporting cells in the optic nerve. Two of these, the oligodendrocyte and the astrocyte, are derived from the neuroectoderm and are referred to as neuroglia (fig. 2). The third element is the reticuloendothelial representative to the nervous system. This cell, the microglia, probably is of mesodermal origin.

Oligodendrocytes are concerned with metabolism of myelin. Hence, they correspond to the Schwann cells of true peripheral nerves. The presence of oligodendrocytes instead of Schwann cells is one of several features which the optic nerve has in common with fiber tracts of the brain. Oligodendrocytes do not have the regenerative capacity possessed by Schwann cells. Therefore, pathologic processes which destroy oligodendrocytes along with myelin sheaths cause irreparable damage.

Astrocytes (fig. 2) furnish structural and nutritional reinforcement to the nerve. They have long fibrous processes, one of which usually passes to the periphery of the nerve bundle, where it fans out to form a limiting membrane separating the neurectodermal structures from the pial septums (fig. 1, B). In the retrobulbar portion of the nerve, astrocytes are less numerous than oligodendrocytes. Within the ocular segment of the nerve, astrocytes become more numerous. Here they contribute to the structure of the lamina cribrosa, form the border tissue of Jacoby, the intermediate tissue of Kuhnt, and Elschnig's central tissue meniscus.

Microglia are present in small numbers and are most difficult to demonstrate in normal nerves (fig. 2, D). However, within short periods after many kinds of damage they become very numerous and

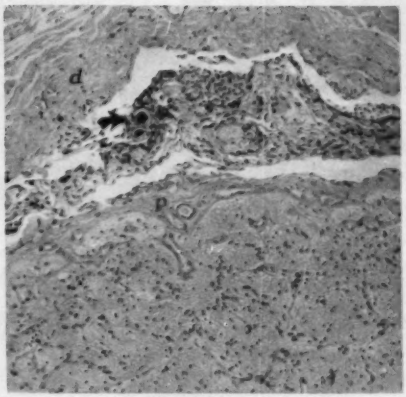

FIG. 3—AFIP Acc. 684100. Normal meninges of optic nerve: the dura (d) is a thick collagenous sheath with relatively few cells and blood vessels; the arachnoid (a) contains meningothelial cells and psammoma bodies (arrow); the pia (p) is intimately adherent to the nerve and by its extensions carries the main blood supply into the nerve. (H & E, × 100)

conspicuous. They possess phagocytic abilities in common with macrophages elsewhere in the body.

The meninges need be mentioned only briefly (fig. 3). Dr. Henderson has described their gross anatomy. Important here is a consideration of the pial extensions which subdivide the nerve into compartments for its large bundles. Each extension of pia into the nerve carries with it small blood vessels. These anastamose with other pial vessels and also with those vessels accompanying the central retinal artery and vein. In the normal nerve, particularly in young individuals, the pial tissue enclosing these small vessels is exceedingly delicate (fig. 4, A). The collagen fibers of the pia become more abundant and coarser with advancing age (fig. 4, B). Thus the septal vessels acquire a thicker connective tissue sheath, which may interfere with exchange of oxygen and nutrients in old age.

Micro-organisms and inflammatory cells in the pia and arachnoid may extend into the nerve via these pial septums

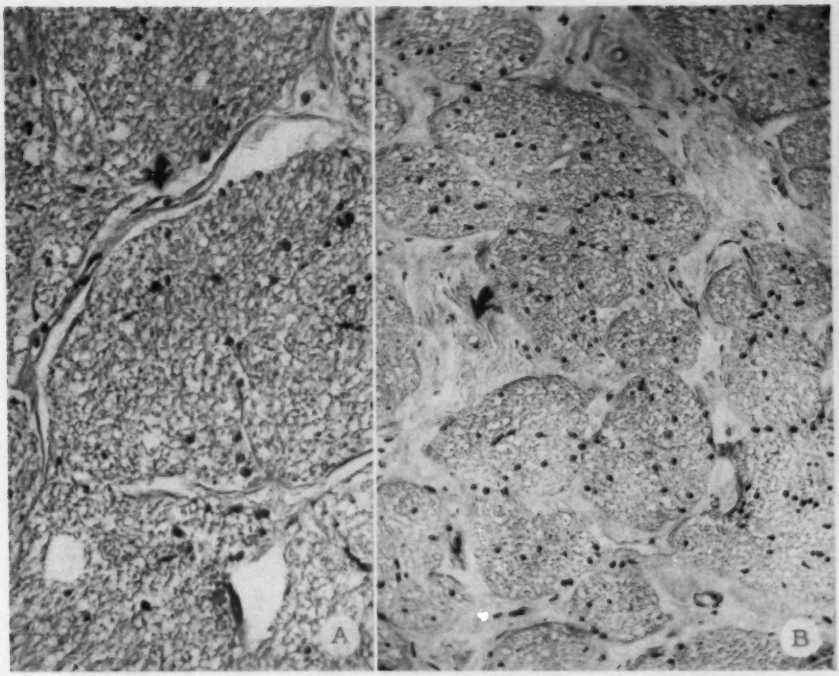

FIG. 4—(A) AFIP Acc. 114419. Normal optic nerve of a 26-year-old soldier showing virtual absence of connective tissue about septal vessels (arrow). (H & E, × 265) (B) AFIP Acc. 618132. Optic nerve of a 78-year-old man. The septal vessels (arrow) have a thick mantle of collagenous connective tissue. (H & E, × 160)

(fig. 5). At first there is only a perineuritis. If with extension of the inflammatory process into the pial septums, the physiology of the peripheral nerve bundles is damaged, then a contraction of the peripheral visual field may be found. The arachnoid has interesting proliferative tendencies. Some are reactive, some neoplastic.

At the lamina cribrosa the diameter of the nerve diminishes because the fibers lose their myelin sheaths (fig. 6). This is important to keep in mind because in atrophic nerves with destroyed myelin sheaths, the diameter of the nerve posterior to the lamina may be so reduced that it becomes smaller than the diameter at the lamina. As a result of this shrinkage of nerve tissue, the subarachnoid space is widened. In a horizontal section through the normal nerve head, the nasal half appears bulkier, and it contains the largest branches of the central vessels. This must also be borne in mind lest the smaller, less vascular temporal half be considered atrophic.

PAPILLEDEMA

Tissue fluids are thought to flow backwards from the eye through the papilla into the nerve. Any alteration in pressure relationships between that within the eye and that within the nerve sheaths causing a diminished flow of tissue fluids into the nerve from the eye will predispose to swelling of the papilla. If there

is, in addition, compression of the central vein as it traverses the subarachnoid space, this will further diminish the rate of fluid resorption from the nerve head. There may also be increased loss of fluid from the dilated capillaries of the nerve head.

nisms: displacement, compression, and separation of the retina about the disc. Most important is the displacement of retinal tissue away from the disc margins (fig. 9). Sometimes the retina remains fairly well anchored to the disc margins, but the swollen nerve fibers

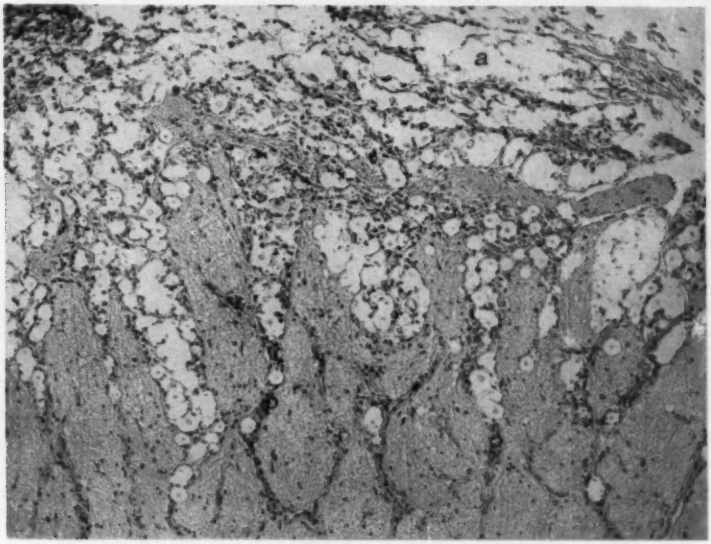

FIG. 5—AFIP Acc. 176358. Optic neuritis in a case of cryptococcal meningoencephalitis. The fungous cells invade the nerve by extending along the pial septums (p) from the arachnoid (a). (H & E, × 75)

When excessive interstitial fluid accumulates in the nerve head, the nonmyelinated fibers take up some of this fluid, becoming swollen and tortuous. The outer fibers of the disc show the earliest and most accentuated swelling and tortuosity (fig. 7). Later the inner fibers are affected. The anterior glial fibers of the lamina cribrosa are bowed forward and separated from the posterior scleral fibers (fig. 8), and there is narrowing of the physiologic cup.

Enlargement of the blind spot due to papilledema is effected by three mecha-

radiating from the nerve head compress the underlying retinal tissue. Finally there may be a peripapillary detachment of the retina accompanying papilledema (fig. 10). Microscopically there is little else to be seen besides increased vascularity and edema. There is a noteworthy absence of inflammatory cells.

With prolonged papilledema, there may be secondary degenerative changes. Varicosities and cytoid bodies (fig. 11, A) develop in the myelinated fibers of the disc. Chromatolysis may be observed in the ganglion cells. One of the most

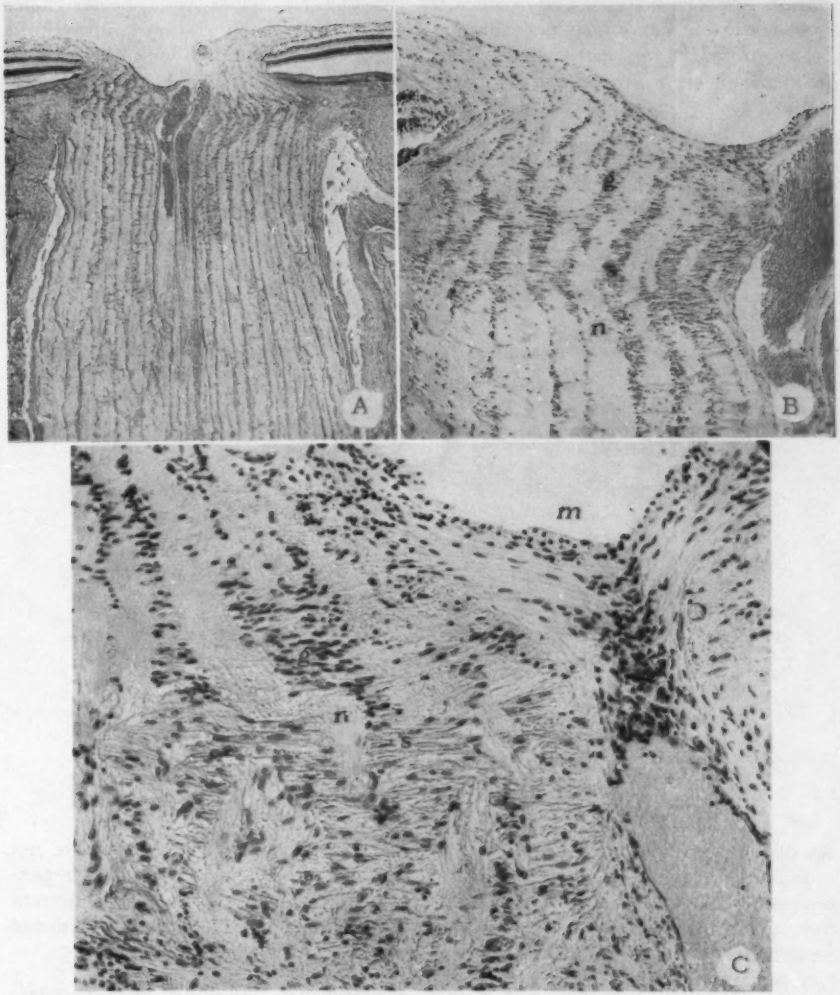

FIG. 6—(A & B) AFIP Acc. 140999. Normal optic nerve head sectioned longitudinally in horizontal plane. The temporal side, seen on the left in (A), is normally less bulky and less vascular than the nasal side. Because of its loss of myelin sheaths, the optic nerve has a diminishing caliber anterior to the lamina cribrosa. An enlargement of the photograph of the temporal side (B) shows the orderly orientation of nerve fiber bundles (n) as they pass through the scleral (s) and glial (g) portions of the lamina cribrosa. (C) AFIP Acc. 219949. The structure of the lamina cribrosa is shown at a greater magnification, and the specialized glial cells lining Elschnig's central tissue meniscus (m) are demonstrated. (A) × 23; (B) × 70; (C) × 150; all, H & E.

readily recognized changes of longstanding papilledema is the proliferation of fibrous astrocytes (fig. 11, B). Since it is believed that nerve fiber degeneration is a stimulus for astrocytosis, pronounced gliosis in an edematous nerve head may be taken as evidence that there has been damage to the nerve fibers. Gliosis is most intense where astrocytes are normally most numerous (e.g., in Kuhnt's intermediate tissue). Shrinkage of fibrous astrocytes may play a role in pulling the displaced retina back into position, and retraction of these glial cells causes the once swollen disc to become flattened. The blind spot, however, may remain enlarged because of permanent damage of the juxtapapillary retina.

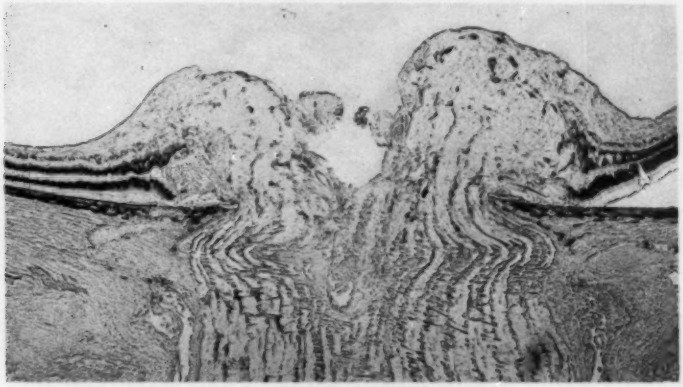

FIG. 7—AFIP Acc. 283414. Papilledema due to metastatic carcinoma of brain. The earliest and most pronounced swelling is observed about the periphery of the disc, where the swollen fibers displace the retina away from the normal disc margins. There is also forward protrusion of the nerve head against the vitreous, as a result of which the physiologic cup appears narrow and deep. Compare with normally shallow and broad cup shown in figure 6. (H & E, × 28)

OPTIC NEURITIS, PAPILLITIS AND NEURORETINITIS

In his introductory remarks, Dr. Carroll indicated that whenever these terms are used by members of this panel, it is understood that there is impaired function. However, the pathologist looking at a microscopic section cannot always be certain that lesions he designates as neuritis, papillitis, or neuroretinitis are actually associated with defective vision. This discrepancy accounts for certain disc changes which clinically are regarded as papilledema (because of preserved function) but which on microscopic examination show mild inflammation, and are therefore labelled as papillitis by the pathologist. These are not to be regarded as fundamental discrepancies; rather, they represent the different criteria and nomenclature which clinician and pathologist must follow.

Frequently the suffix "itis" is interpreted to imply infection; for this reason the use of this term for noninfectious diseases has been unjustly criticized. Actually "itis" means inflammation, and this may be secondary to many different types of insult besides infection. Hence, there should be no serious objection to consideration of degenera-

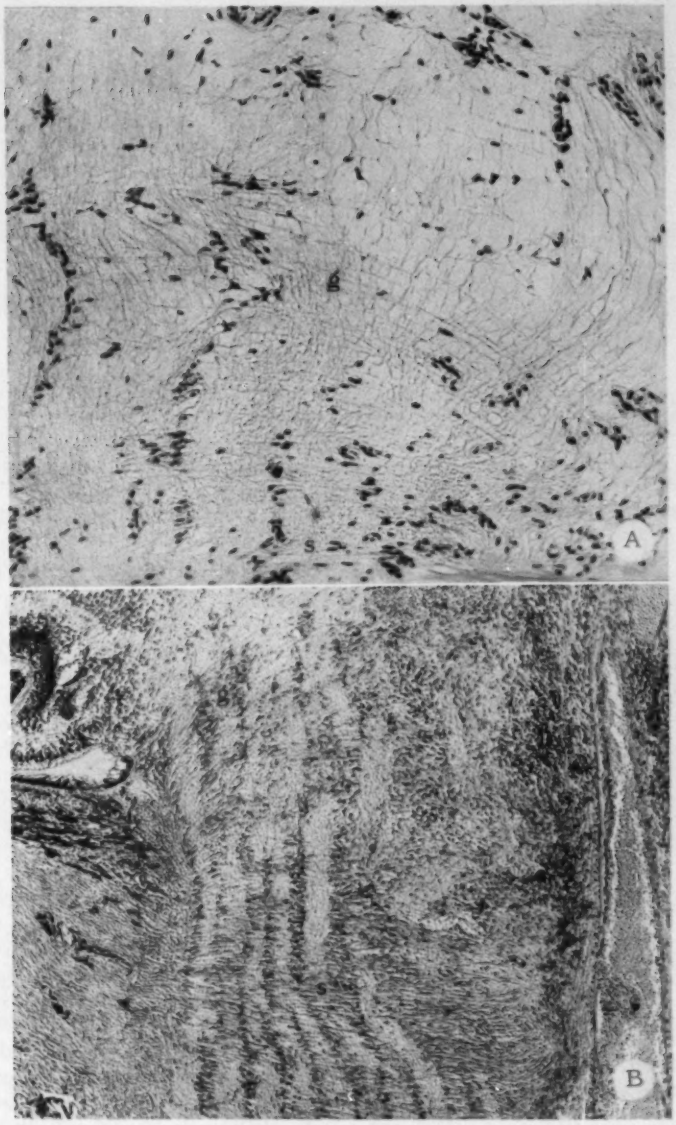

FIG. 8—(A) AFIP Acc. 283414. In the edematous nerve head, the glial (g) component of the lamina cribrosa may be bowed forward away from the more rigid scleral (s) fibers. (B) AFIP Acc. 219940. The same process is observed in a case of papillitis. (A) × 140; (B) × 68; both, H & E.

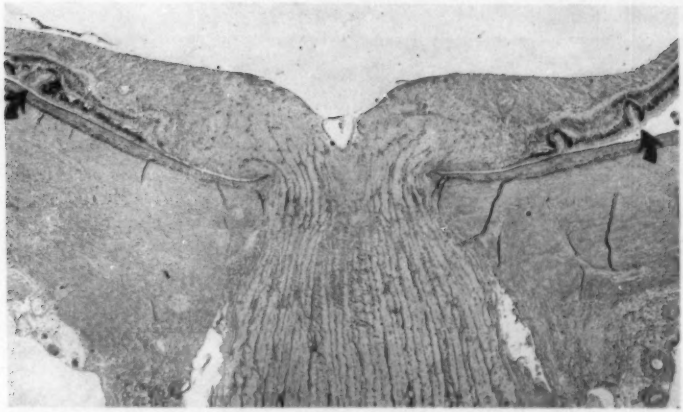

FIG. 9—AFIP Acc. 185418. Papilledema due to hypotony (penetrating wound). Regardless of specific cause, the histologic features of papilledema are fairly constant. The retina is displaced away from the normal disc margins. It therefore tends to buckle (arrows). The retina is also compressed by the swollen nerve fiber layer adjacent to the disc. All of these are factors that account for the enlarged blind spot characteristic of papilledema.

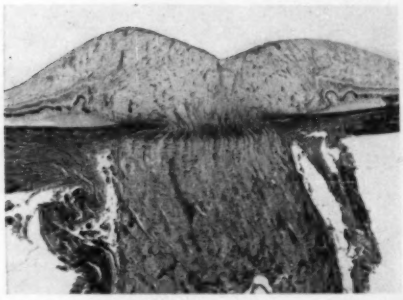

FIG. 10—AFIP Acc. 210154. Papilledema due to metastatic osteogenic sarcoma. There is peripapillary retinal separation with the accumulation of serous exudate between the percipient elements and the pigment epithelium. Note that displacement, buckling, and compression of retinal tissue are also present. (H & E × 17)

tive, nutritional, toxic and vascular disorders under the general heading of optic neuritis.

From the viewpoint of the pathologist, the most common type of optic neuritis is secondary to processes affecting adjacent structures. These are principally infections or tumors of the eye, orbit, bony canal, paranasal sinuses, or meninges. Often in such cases the primary process so dominates the clinical picture that optic nerve involvement is not appreciated. Although infections of the optic nerve are usually caused by direct extension from adjacent structures (figs. 5 and 12), blood-borne infection may also occur (fig. 13).

In all of these infectious processes, the character of the inflammatory reaction observed in the optic nerve varies with the properties of the responsible micro-organism and whether or not the organism is actually in the nerve or in its sheaths. In many cases, particularly those of papillitis secondary to intraocular disease, the changes we observe in the nerve head are apparently due to a diffusion of toxins from other parts of the eye into the nerve head. In these cases the principal histologic changes are dilatation of blood vessels, edema of the disc and adjacent retina, perivascular cuffing by lymphocytes, and proliferation of astrocytes (fig. 14).

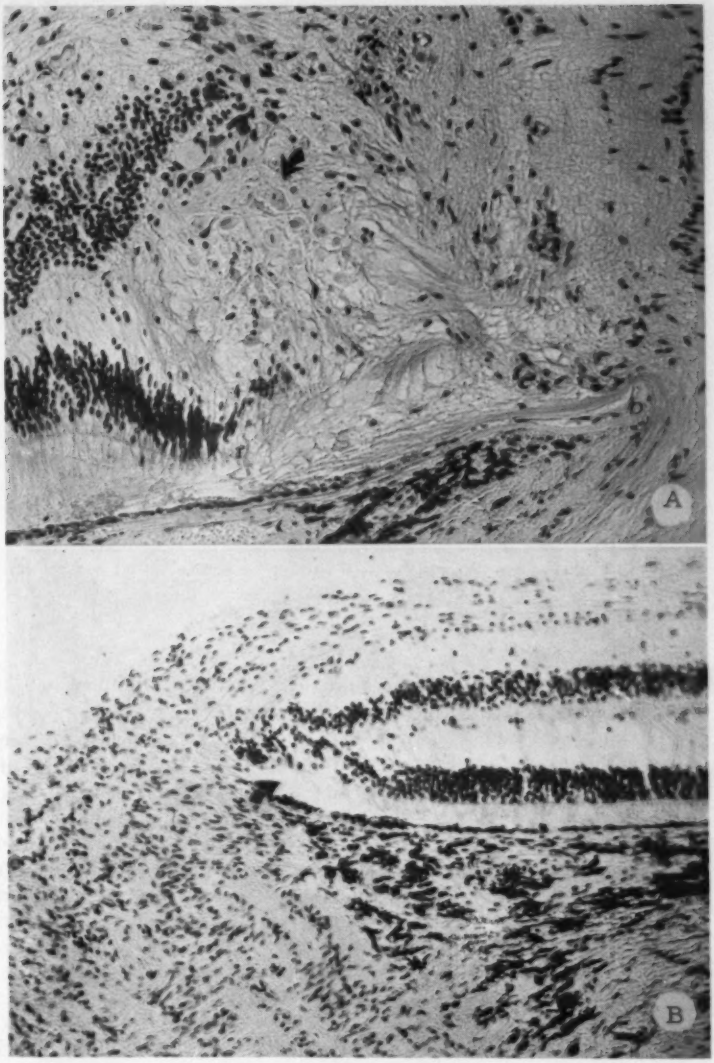

FIG. 11—(A) AFIP Acc. 283414. Same case as that shown in figure 7. Degenerative changes, including the formation of cytoid bodies (arrow) are observed in the swollen nerve head. To appreciate the degree of retinal displacement that has occurred, it must be realized that the end of the retina (r) normally is in apposition with the end of Bruch's membrane (b); compare with figure 6. (B) AFIP Acc. 265065. With degeneration of nerve fibers, there is a great increase in the number of glial cells throughout the nerve head and adjacent retinal nerve fiber layer. Although the edema has subsided and the retina is back in place, there is permanent damage, with loss of percipient cells (arrow) at the disc margin. (A) and (B), H & E; × 160.

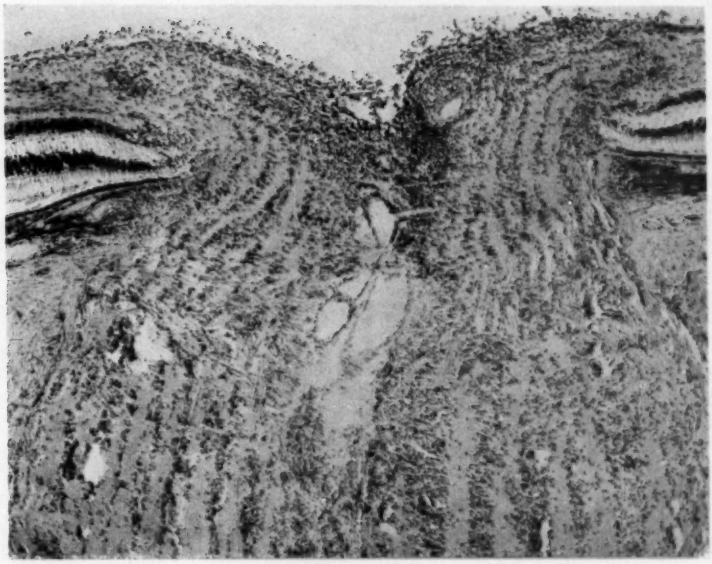

FIG. 12—AFIP Acc. 37670. Papillitis in a case of ocular toxoplasmosis. (H & E, × 48)

If micro-organisms actually gain access to the nerve or its sheaths, the reaction observed may run the gamut from pyogenic (as with most bacterial meningitides and some fungous infections) to chronic granulomatous (as in tuberculosis and most fungous infections).

In the noninfectious types of optic neuritis, we seldom have the opportunity for pathologic study during the acute phases of the process. Most of these diseases are not fatal, and by the time the patient comes to autopsy there has either been recovery or the process has progressed to atrophy.

I therefore plead, in the event that one of your patients with optic neuritis should die unexpectedly as a result of trauma or intercurrent disease, that you make every possible attempt to obtain the eyes, optic nerves, chiasm and brain at autopsy.

OPTIC ATROPHY

Atrophy is a general term used by the morphologist to indicate an acquired diminution in size—a shrinking of cells or fibers which have reached their full development. To the physiologist and clinician, there is the implication of decreased function. Thus optic atrophy may be the end result of a wide variety of lesions. When the primary lesion is located in the eye, we speak of an "ascending atrophy" of the nerve (fig. 15). This is of little concern to us in the present discussion, since in such cases it is the primary intraocular lesion which dominates the picture. Of especial importance to us, however, is "descending atrophy" due to lesions located within the cranium or in the orbital segment of the nerve. In such instances, the disc may appear completely normal at first, but ultimately the nerve head becomes atrophic (fig. 16) and even the retinal

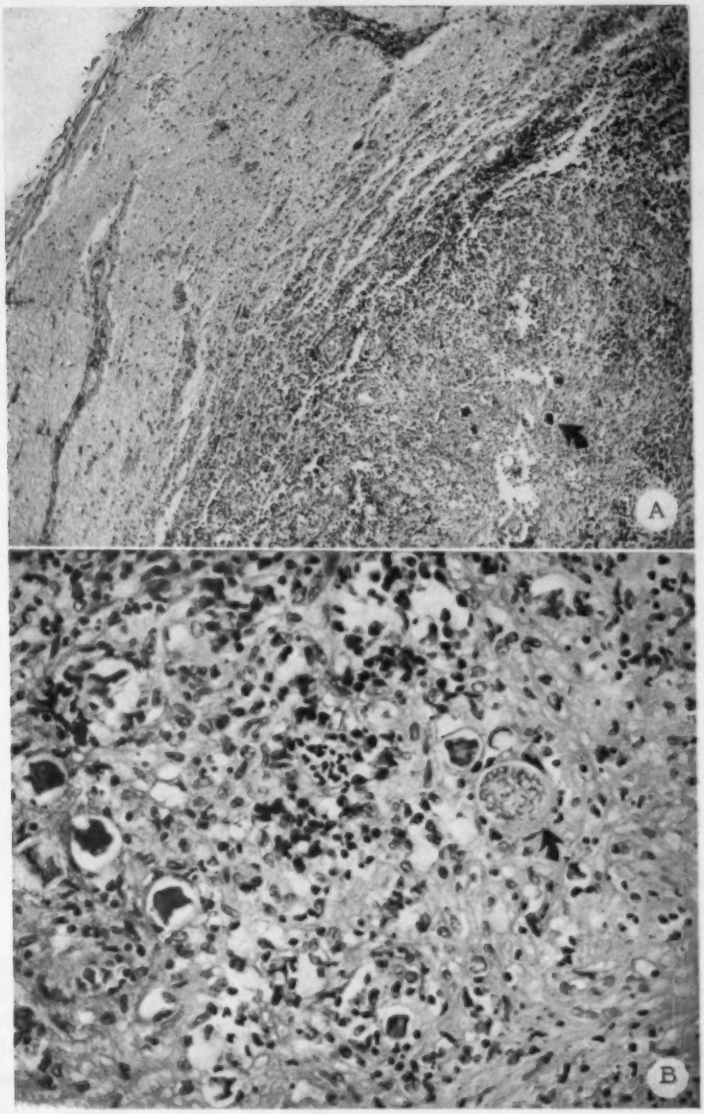

FIG. 13—AFIP Acc. 114120. Granulomatous optic neuritis in a case of disseminated coccidioidomycosis. (A) Crenated spherules (arrow) may be seen in the center of the granuloma even at low magnification. (H & E, × 70) (B) Endosporulating sporangia are also present (arrow). (H & E, × 300)

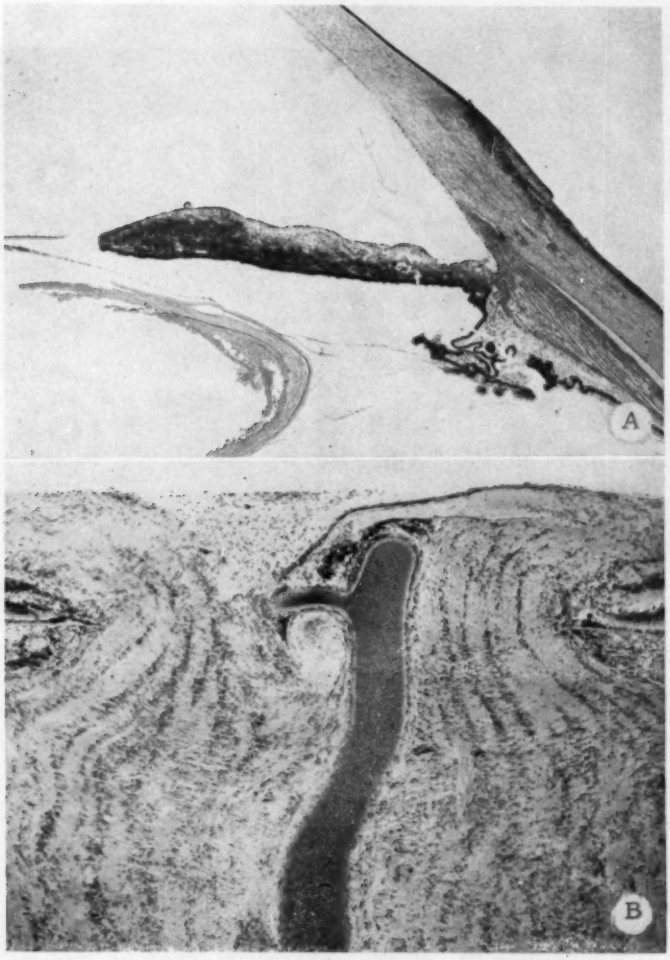

FIG. 14—AFIP Acc. 219939. Nonspecific papillitis associated with chronic nongranulomatous iritis. The nerve head is engorged and slightly edematous. There is mild perivascular cuffing by lymphocytes and the physiologic cup is filled in with mesodermal tissue. (A) × 20; (B) × 55; both, H & E.

ganglion cells may disappear (fig. 16, D). Such changes are observed earlier when the lesion is close to the globe.

The ophthalmoscopic appearance of the disc in optic atrophy is dependent upon a number of factors. Atrophy per se contributes by virtue of the diminished tissue volume and lesser vascularity. More important, however, are those secondary proliferative changes involving neuroglia, blood vessels, and fibroblasts. In descending atrophy, as, for example, with intracranial neoplasms or in tabes dorsalis, there is a slow orderly replace-

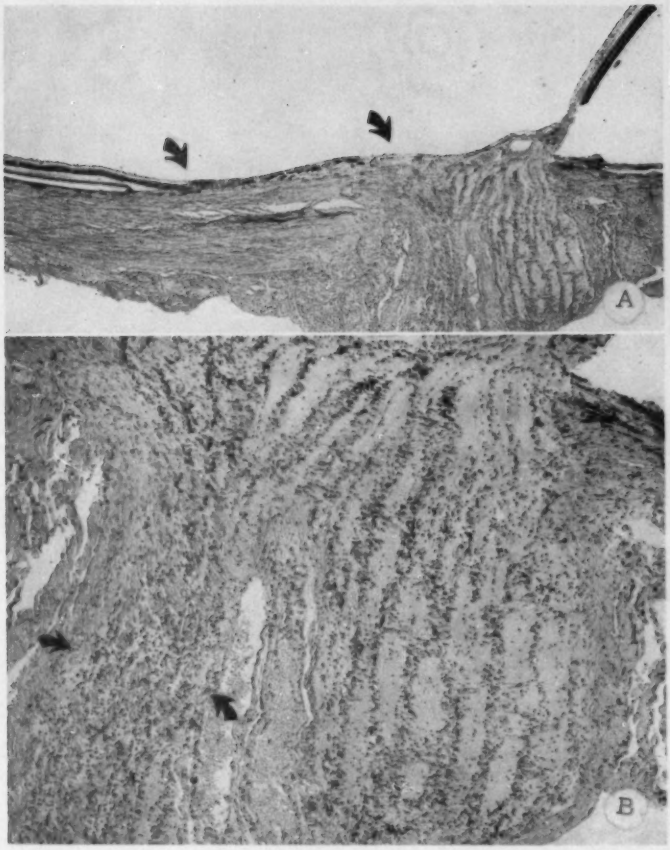

FIG. 15—AFIP Acc. 198429. Ascending optic atrophy secondary to an extensive juxtapapillary chorioretinal scar (arrows) on the temporal side. The degree of optic atrophy is appreciated best by comparing the size and arrangement of nerve bundles on the temporal (left) side of the central vessels with those on the uninvolved nasal (right) side. (A) × 21; (B) × 50; both, H & E.

ment of nerve fibers by astrocytes, and mesodermal reaction is negligible (fig. 16). The ophthalmoscopic appearance of the disc in such cases is that of simple (so-called primary) optic atrophy. On the other hand, following papillitis there may be a more haphazard astrocytosis accompanied by a striking mesodermal reaction. These secondary proliferative processes account for the ophthalmoscopic changes, which are designated secondary optic atrophy. In such cases, the physiologic cup may be filled and the entire disc covered by a new growth of capillaries and connective tissue (fig. 17). Hemorrhages may occur from this vascular tissue, and this in turn serves as added stimulus to more fibrovascular proliferation. Disc changes may also be observed following papilledema. Nerve

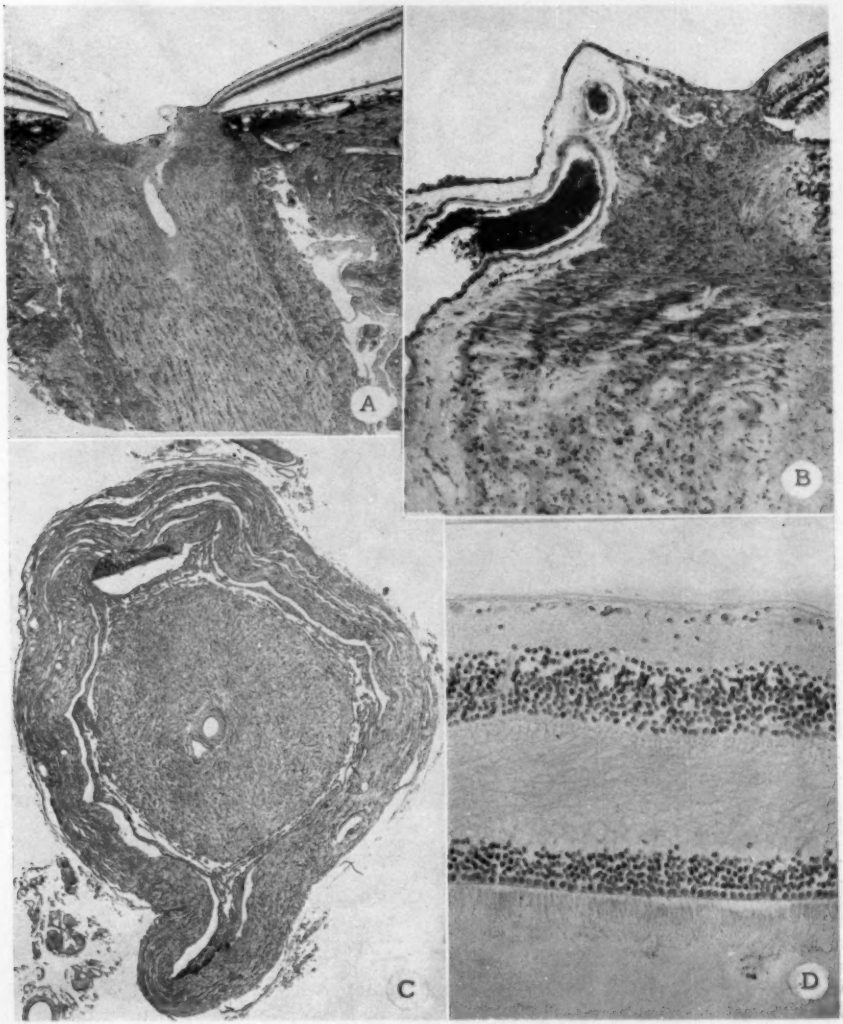

FIG. 16—AFIP Acc. 290829. Descending optic atrophy in tabes dorsalis. (A) There is pronounced wasting of the optic nerve and disc, as a result of which the caliber of the nerve is considerably less just posterior to the lamina cribrosa than at the lamina (compare with normal in figure 6,A). Because of the lesser bulk of the nerve head, the physiologic cup is enlarged. The lack of glial and mesodermal raection in these slowly progressive descending atrophies secondary to intracranial lesions is demonstrated in (B). With the loss of nerve tissue and minimal replacement by glia, the caliber of the nerve as seen in cross section (C) is greatly reduced, while the unchanged meninges become redundant (compare with figure 3). The effect of descending atrophy extends to the retina (D) where the architecture is preserved except for the almost complete loss of nerve fiber layer and ganglion cells. (A) ×20; (B) ×80; (C) ×20; (D) ×185; all, H & E.

FIG. 17—AFIP Acc. 189997. The case illustrated was one of iridocyclitis and optic neuritis believed to be due to syphilis; there was also secondary glaucoma. The appearance of the optic nerve head is altered by the intense mesodermal reaction. An inflammatory membrane covers the disc and adjacent retina. Hemorrhage has occurred from this membrane, and a layer of blood clings to it. (H & E, × 25)

fiber degeneration excites an astrocytic response. Irregular peripapillary detachment of the retina also contributes to the irregularity of the disc margins observed after papilledema.

Finally, a word about cavernous atrophy (fig. 18). In this type of atrophy, the atrophic nerve fibers are replaced neither by glial nor by mesodermal connective tissue, but by fluid. When the tissue is sectioned, this fluid escapes, leaving cavernous spaces — hence the name.

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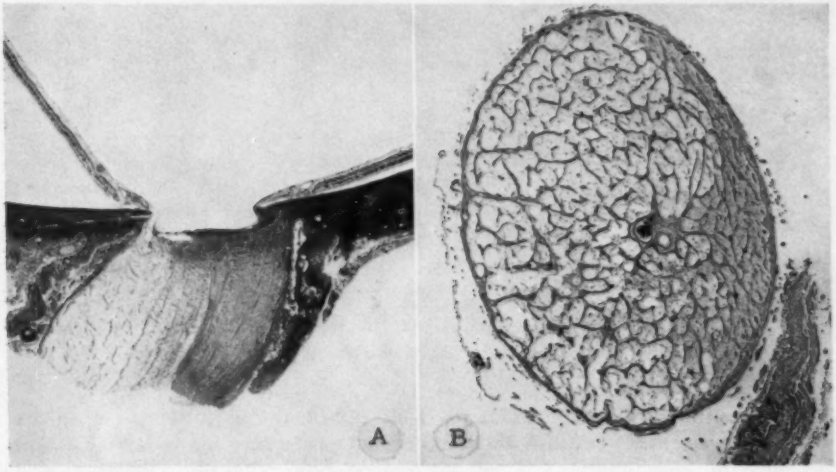

FIG. 18—(A) AFIP Acc. 105049. (B) AFIP Acc. 283289. When the atrophic nerve bundles are replaced by fluid, the histologic picture of cavernous optic atrophy is produced. (A)×12; (B)×20; both, H & E.

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III

ETIOLOGIC CLASSIFICATION

FRANK D. CARROLL, M.D.

OPTIC nerve disease may be caused by any of the following disorders:

1. Inflammation in adjacent structures
2. Systemic infection
3. Multiple sclerosis and allied diseases
4. Hereditary affections
5. Circulatory disorders
6. Trauma
7. Generalized noninfectious diseases
8. Malnutrition
9. Toxicity
10. Tumors
11. Unknown disorders

The panel has agreed on this classification of optic nerve disease, which it considers logical and simple. There is much that is known, and much of course that is still unknown, about each of these categories. Let us proceed with what is known about the first of them—spread of inflammation from adjacent structures—which will be discussed by Dr. Henderson.

IV

SPREAD OF INFLAMMATION FROM ADJACENT STRUCTURES

JOHN WOODWORTH HENDERSON, M.D.

INVOLVEMENT of the optic nerve by extension from neighboring structures may be classified as follows:

1. Intraocular
2. Intraorbital
3. Intracanalicular
4. Intracranial

Intraocular Structures

Intraocular inflammations will occasionally affect the optic nerve. The constant response is some degree of swelling of the nerve head (fig. 1). This may occur by direct extension from a choroiditis or retinitis, in which case the field defect is of the nerve-fiber bundle type. Swelling of the nerve head, accompanied by a central scotoma, occurs in anterior uveitis. In certain cases, an iridocyclitis may be associated with a central scotoma in the same eye without visible macular or disc change, suggesting retrobulbar neuritis.[4] Posterior sympathetic ophthalmitis is an infrequent cause of disc swelling with associated central visual loss.

Intraorbital Structures

Orbital cellulitis may arise from pyogenic infections of the face with intraorbital extension or from metastatic infection. Mucormycosis has also been reported as a cause of such infection (fig.

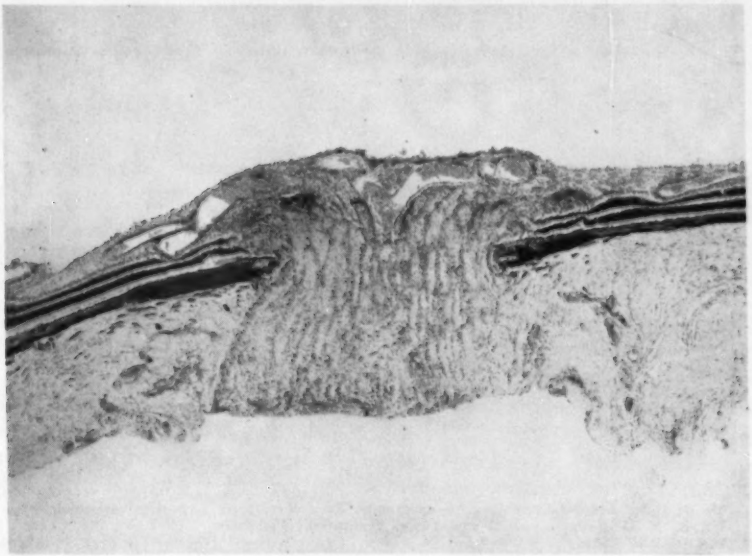

FIG. 1—Papillitis in purulent endophthalmitis. (H & E; × 27) (Courtesy of Armed Forces Institute of Pathology.)

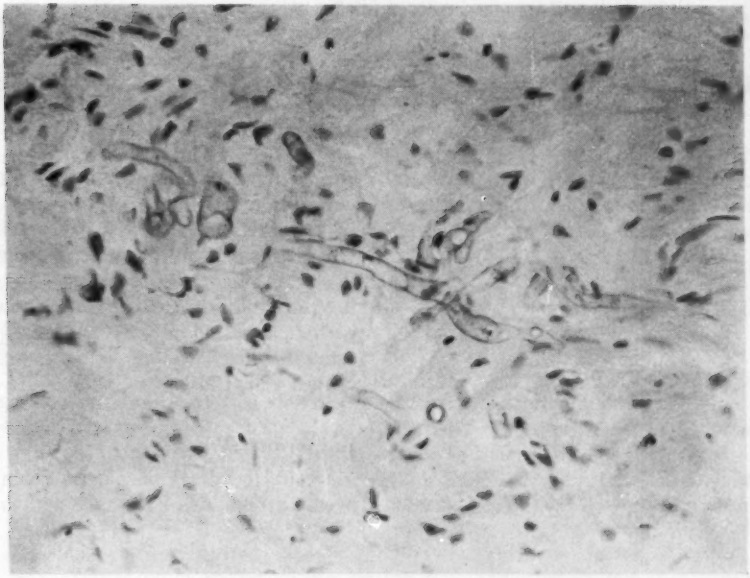

FIG. 2—Mucor within optic nerve. (H & E; × 300) (Courtesy of Armed Forces Institute of Pathology.)

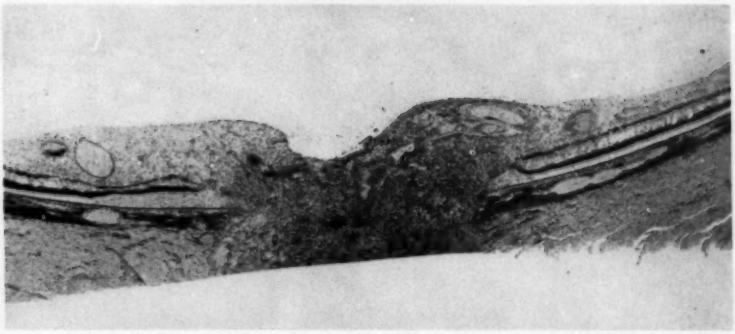

FIG. 3—Optic neuritis secondary to cavernous sinus thrombosis and purulent meningitis. (H & E; × 25) (Courtesy of Armed Forces Institute of Pathology.)

2).[3] Direct spread may then involve the optic nerve. More frequently, the source of such orbital infections is extension from a purulent paranasal sinusitis (fig. 3). When orbital cellulitis is present, there can be little doubt as to the etiologic relationship of sinus infection to optic neuritis. However, cases with the clinical picture of retrobulbar neuritis and associated localized sinus disease are

rare. Since a high percentage of such cases improve without surgical intervention, the cause and effect relationship of cure from surgery is tenuous. While it is undoubtedly true that direct extension of a frankly suppurative sinusitis may involve the optic nerve, the panel believes that attempts to relate lesser degrees of sinus involvement to optic neuritis are seldom justified.

A rare and recently described condition, Wegener's granulomatosis, has been shown to affect the optic nerve as a part of its orbital involvement (fig. 4). This lethal midline granuloma, of unknown etiology, is an inflammatory granulomatous process involving the upper respiratory tract and progressing to ulceration and gangrenous necrosis of soft and osseous tissues.[2] The granuloma either compresses the optic nerve or interferes with its blood supply by a necrotizing angiitis (fig. 5).

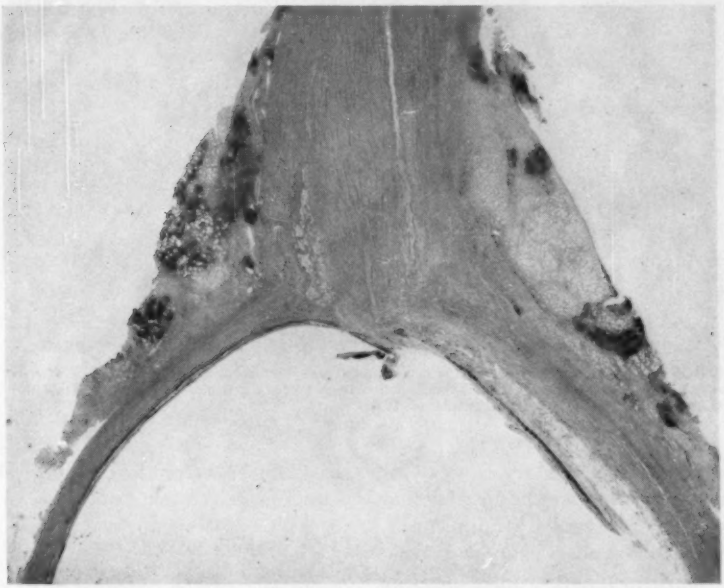

FIG. 4—Orbital involvement about optic nerve in Wegener's granulomatosis. (H & E; × 7.5)
(Courtesy of Armed Forces Institute of Pathology.)

Intracanalicular Structures

Within the optic canal it is possible for osteitis to extend to the nerve and to produce eventual optic atrophy.[1] If periostitis of the superior orbital fissure extends to the optic foramen, an optic neuritis may be added to the motor and sensory signs already present. Since there is little room for expansion within the canal, any edema of the nerve will quickly result in a conduction block and, later, to degeneration.

Intracranial Structures

Intracranial involvement of the optic nerve usually results from an inward ex-

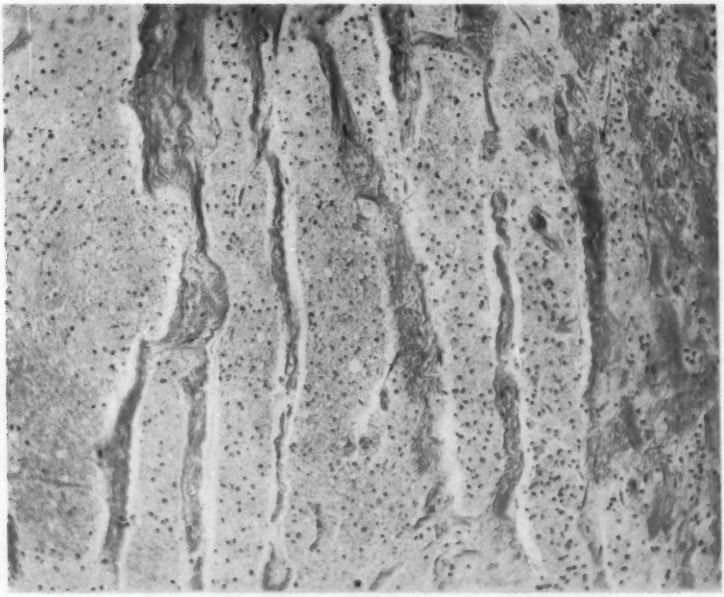

FIG. 5—Complete necrosis of optic nerve bundles, probably secondary to occlusion of arterial supply incident to extensive orbital inflammation in Wegener's granulomatosis. (H & E; × 80) (Courtesy of Armed Forces Institute of Pathology.)

tension of an inflammatory process involving the meninges. The usual lesion is a perineuritis. Middle ear infections, infection after skull fracture, epidemic cerebrospinal meningitis, tuberculous or syphilitic meningitis, or other bacterial or mycotic meningitides may extend in this way. The visual fields usually show peripheral contraction (fig. 6).

Intracranial optic nerve involvement has been reported many times as a part of the clinical picture of optico-chiasmatic arachnoiditis. The panel believes that this is a rare condition. The diagnosis can be made during surgical exploration for possible tumor.

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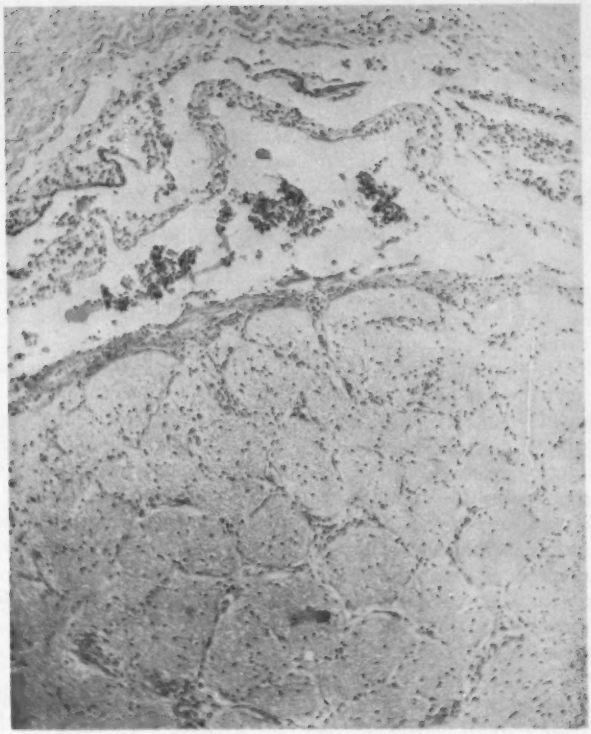

FIG. 6—Degeneration of peripheral optic nerve fibers in purulent meningitis. (H & E; × 75) (Courtesy of Armed Forces Institute of Pathology.)

V

DISEASE SECONDARY TO SYSTEMIC INFECTION

JOHN WOODWORTH HENDERSON, M.D.

IT is difficult to determine in the majority of cases whether optic nerve involvement in the course of a systemic infection is the direct result of the infective agent or whether it is a part of a toxic encephalomyelitis. The difficulty may be compounded by factors of nutrition and tissue sensitivity, which may also play a role. Nevertheless, optic nerve involvement has been reported as an incidental complication in almost all infections.[12] The more important ones will be considered.

A. *Bacterial Infections*

1. Scarlet fever—optic atrophy occurs rarely.
2. Erysipelas—orbital cellulitis with optic neuritis has been reported.
3. Pneumonia — a low-grade blurring of the discs has been noted.[15] Optic neuritis is rare.
4. Diphtheria — rarely, optic neuritis occurs.
5. Epidemic meningitis — direct spread produces a perineuritis with optic atrophy in some cases. In patients with transient bilateral visual loss resulting in no pallor of the discs, the visual defect is probably cortical.
6. Tularemia — optic atrophy has been reported.
7. Pertussis — optic neuritis and atrophy occur rarely.
8. Plague—optic neuritis is rare.
9. Enteric diseases—typhoid fever is said to cause optic neuritis more frequently than any other infectious disease; atrophy may follow. Optic atrophy has been reported in bacillary dysentery.
10. Brucellosis—choked disc in the acute cases is apparently secondary to meningeal involvement. Optic neuritis[14] as well as optic atrophy[2] has been noted.
11. Tuberculosis—as a complication of tuberculous meningitis, optic neuritis not infrequently occurs. Six cases of bilateral optic atrophy were found in 108 proved cases of tuberculous meningitis in a recent survey in Baltimore.[16] These patients had all been treated with streptomycin or other specific antibiotic drugs, thus surviving to demonstrate optic nerve damage.
12. Sarcoidosis—cases have been reported with optic nerve involvement. In uveoparotid fever, bilateral papilledema preceding the uveitis has been noted.[10] This was thought to be due to a localized area of meningitis involving the superior orbital fissures.
13. Syphilis — will be discussed by Dr. Walsh.
14. Leptospirosis—optic neuritis has been reported.
15. Focal infection—occasional cases have been reported, but the etiologic relationship is unresolved.

B. *Virus Infections*

The panel has agreed to consider the optic nerve involvement following certain viral infections under the heading of demyelinating diseases. These will be discussed by Dr. Rucker.

1. Herpes zoster ophthalmicus—in a complete review of the literature,[5]

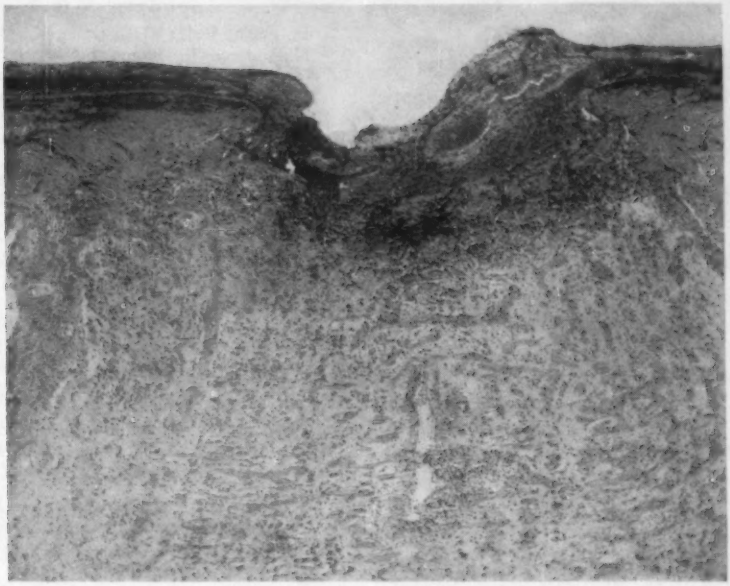

FIG. 1—Optic neuritis associated with herpes zoster. (H & E; × 42) (Courtesy of Armed Forces Institute of Pathology.)

it was found that 1.8 per cent of the cases evidenced retrobulbar neuritis, optic neuritis, or optic atrophy (fig. 1). Individual cases of retrobulbar neuritis have also been reported in recent years.[9] It is thought that extension occurs directly from the trigeminal nerve to the optic nerve.

2. Virus infection (la grippe)—optic neuritis can occur as a complication of influenza,[12] and in certain epidemics it may be more frequent than in others. In one influenza epidemic, optic neuritis was associated with minimal spinal cord symptoms in at least 3 cases.[2]
3. Poliomyelitis—it has been reported that papilledema occurs in almost 5 per cent of cases, usually in the convalescent stage,[17] but it seems doubtful that a true papillitis occurs. The disc edema may be dependent on an increased cerebrospinal fluid protein level with marked perivascular lymphocytic infiltration.[8] A single case of bilateral optic neuritis in a child with poliomyelitis, proved by monkey inoculation, has been reported.[1]

(The following entities are presumed due to virus infection, but an etiologic agent has not been proved.)

4. Acute benign lymphocytic meningitis—acute optic neuritis as well as papilledema has been reported.
5. Infectious mononucleosis — optic neuritis definitely occurs in this disease. Bilateral visual loss and associated ophthalmoplegia have been seen.[16] The true incidence of optic nerve involvement is not known, since many patients do not have an adequate ocular examination.[13]

6. Guillain-Barré syndrome — although papilledema has been reported together with blurred vision,[4] evidence of a clear-cut optic neuritis is lacking.

C. *Parasitic Infections*

1. Malaria—papillitis is said to occur more frequently than retrobulbar neuritis, although both are uncommon.[7] In one series, optic neuritis was reported in 2 per cent of cases. Visual loss, with scotomas and blurring, may be central in origin as well as peripheral. Such visual involvement must be carefully differentiated from quinine amblyopia.

2. Onchocerciasis—retrobulbar neuritis due either to direct microfilarial involvement or to toxins from the adult worm has been reported.[11]

3. Toxoplasmosis—optic neuritis has been seen in a few cases of congenital toxoplasmosis.[6] Infants born during the "late" stage of the infection in the mother had severe cerebral involvement, as manifested by roentgen studies and by neurologic tests.

D. *Mycotic Infections*

As noted earlier, mucormycosis may attack the optic nerve by extension from an orbital cellulitis. Central nervous system torulosis leads to papilledema and visual loss[3]; infiltration can be demonstrated about the optic nerves. In at least 10 per cent of reported cases, torulosis occurs as a complication of Hodgkin's disease. Coccidioidomycosis producing a granuloma of the optic nerve has been seen on pathologic sections.[18]

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VI

SYPHILIS OF THE OPTIC NERVE

FRANK B. WALSH, M.D.
BALTIMORE, MARYLAND

Syphilitic Perioptic Neuritis

As the name implies, syphilitic perioptic neuritis is an inflammatory involvement of the meningeal sheaths of the optic nerve, with the stem of the nerve relatively unaffected. Such cases are rare. Usually they are part of a syphilitic meningitis. There is pronounced swelling of the disc, and the visual acuity remains normal, or nearly so. Differentiation from papilledema is dependent upon demonstration of normal intracranial pressure. The peripheral visual field of the affected eye is normal, or it may possibly show slight concentric narrowing. The blind spot is enlarged. The condition has been bilateral on the few occasions when I have observed it. Penicillin therapy has sufficed. Before penicillin was available, in addition to routine antisyphilitic therapy, malaria was necessary in one case with which I am familiar.

Syphilitic Optic Neuritis and Neuroretinitis

Optic neuritis and neuroretinitis occur infrequently in infants and children suffering from congenital syphilis, according to Igersheimer and in our experience. However, there is not general agreement on this point. Mohr and Beck, also Heine, have said that these conditions are commonly seen in children with congenital syphilis.

Optic neuritis with involvement of the optic disc (papillitis) occurs rarely in early syphilis, but it occurs frequently in the late disease (secondary and tertiary). In most instances optic neuritis is part of a neurorecurrence. There is nothing characteristic about syphilitic optic neuritis to distinguish it from optic neuritis in nonsyphilitic persons in many instances. However, optic neuritis in persons with syphilis may occur when syphilitic uveitis is present. Rather often syphilitic optic neuritis is bilateral. There is, characteristically, swelling of the optic discs and pronounced and rapid loss of vision. The field defects vary within wide limits. With syphilis, lesions have a tendency to be bilaterally symmetrical, and syphilitic optic neuritis offers no exception. With adequate treatment, the prognosis as regards recovery of vision is good.

Syphilitic neuroretinitis is more widespread than optic neuritis. In addition to involvement of the optic disc, the surrounding retina is affected (fig. 1). Often it has a gray appearance. In these cases with or without treatment there is likely to be extreme narrowing of the retinal vessels. In the later stages there is deposition of pigment. The end result is the fundus picture of so-called syphilitic retinitis pigmentosa.

Syphilitic retrobulbar neuritis occurs under several circumstances. It may be (a) part of syphilitic neuroretinitis, (b) part of syphilitic periostitis, (c) in meningitis, or (d) questionably in parenchymatous syphilis. Excluding parenchymatous syphilis (tabes dorsalis, general paralysis of the insane), retrobulbar neuritis accounts for approximately 10 per cent of cases of optic neuritis in syphilitics.

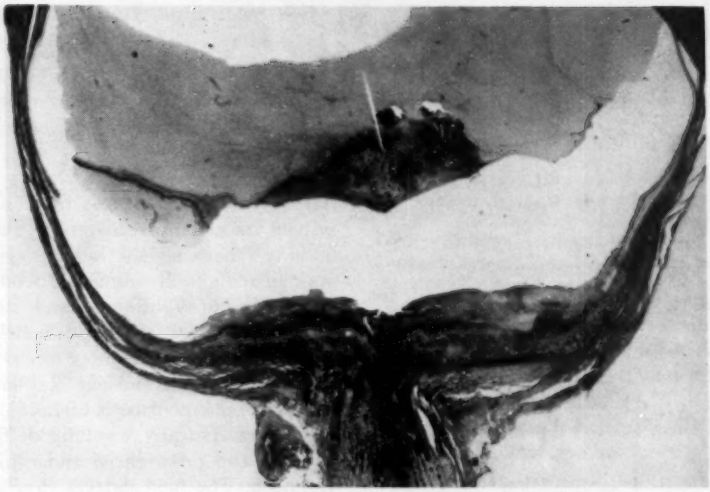

FIG. 1—Syphilitic neuroretinitis.

Excepting in syphilitic neuroretinitis, the prognosis for return of a function is reasonably good if treatment is adequate. Penicillin is the drug of choice. Malaria therapy is an essential addition in refractory cases. Recurrences are particularly frequent with retrobulbar neuritis.

Neuritis Papulosa, Juxtapapillary Chorioretinitis, Gumma of the Optic Disc

These involvements are rare and are difficult to differentiate. Neuritis papulosa is characterized in the terminal stages by a white mass on the disc attached to an atrophic choroidal lesion adjacent to the disc.[3] Syphilitic juxtapapillary chorioretinitis has been observed in the secondary stages of syphilis.[6] It has been associated with involvement of the anterior uvea. Consequently, the eye with juxtapapillary choroiditis may be red, which differentiates it from so-called neuritis papulosa. With the ophthalmoscope, gumma of the optic disc may closely resemble papilledema; vitreous clouding is likely to be present with gumma.

Juxtapapillary chorioretinitis may respond well to penicillin, but neuritis papulosa in its terminal stages responds poorly to treatment. Gumma of the optic nerve responds poorly to therapy.

Choked Discs in Syphilis

Papilledema associated with increased pressure is occasionally the result of syphilis. Either gumma (rare) or intracranial inflammation (meningitis) may result in increased intracranial pressure or papilledema. Ninety per cent of cases of choked disc in syphilitics are due to syphilitic meningitis. Choked discs may be present in congenital or in acquired syphilis. Vision is good, but atrophy of the nerves may supervene.

The diagnosis is made on the basis of a history of syphilis, positive blood and spinal fluid serology, and pleocytosis in the spinal fluid. Brain tumor must be excluded. Adequate treatment leads to recovery, with normal vision in a majority of cases.

Optic Atrophy

In parenchymatous syphilis, the optic atrophy is described as primary, as contrasted with secondary atrophy, which is the type observed as the result of syphilitic meningitis. Primary or simple optic atrophy is characterized by a pale disc, with clear-cut margins, and a normal-appearing optic fundus.

Bruetsch[1] has shown that the optic atrophy associated with parenchymatous syphilis has its origin in an inflammatory process involving the intracranial optic nerves and chiasma. An infiltrative inflammation with an excess of lymphocytes involves both the optic nerve sheaths and the parenchyma of the nerve. Certainly in many instances this process is identical with a syphilitic perineuritis. As the disease progresses, the nerve stem is affected. Because of this intrinsic involvement, surgical attack on syphilitic optochiasmatic arachnoiditis has little or no chance of improving the situation.[2,4] The lesion may be unilateral, but eventually both optic nerves are affected. When one nerve is completely demyelinated, the other already has an inflammatory reaction present in it.

In individuals suffering from optic atrophy of primary type, the visual fields characteristically show peripheral narrowing. In many instances the visual acuity remains remarkably good, often normal, but the narrowing of the field may be extreme. In many cases central visual acuity is materially reduced. Mention has already been made of retrobulbar neuritis being associated with some cases of parenchymatous syphilis. It has been shown that with meticulous field charting, central field defects may be demonstrated in many cases of tabes dorsalis with optic atrophy. Woods and Sloan[7] showed this many years ago. It has not yet been established that in cases of primary syphilitic optic atrophy there ever is a selective involvement of the papillomacular bundle.

Syphilitic optic atrophy as part of parenchymatous syphilis has been considered as almost or altogether resistant to therapy. Unquestionably, intensive treatment improves the outlook greatly in some cases.[5] According to Moore, the pretreatment visual level has prognostic importance. If the vision is 20/60 or better, the outcome has some promise. If it is lower than 20/60, treatment will probably be totally ineffective. If a patient is not blind within three years from the onset of the optic atrophy, the ultimate outcome is reasonably favorable. In the treatment of ocular syphilis, it is imperative that a Jarisch-Herxheimer reaction be avoided. The treatment for optic atrophy consists largely of penicillin, but malaria therapy may also be necessary.

Optic atrophy of the secondary variety may have its origin in syphilis. A syphilitic meningitis may be associated with optic neuritis or with papilledema. In such cases, if there is an associated narrowing of the retinal vessels, the outlook for retaining or regaining normal vision is not good.

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VII

THE DEMYELINATING DISEASES

C. Wilbur Rucker, M.D.
ROCHESTER, MINNESOTA

The group of demyelinating diseases includes multiple sclerosis, neuromyelitis optica (Devic's disease), progressive subcortical encephalopathy (Schilder's disease), and postinfectious encephalitis, all of which exhibit similarities, especially in their pathologic processes. However, it is realized that the tissues of the central nervous system can react to injury by noxious agents in only a limited number of ways and, therefore, that similarity in the pathologic process does not necessarily indicate a similarity in cause of the disease. Among the demyelinating diseases there are many differences in the location and severity of the lesions, in the course of the disease, and probably in etiologic agents. They all affect vision in one way or another, through involvement either of the optic nerves or of the optic radiations.

From the Section of Ophthalmology, Mayo Clinic and Mayo Foundation.

The Mayo Foundation, Rochester, Minnesota, is a part of the Graduate School of the University of Minnesota.

MULTIPLE SCLEROSIS

Multiple sclerosis is a chronic remitting disease of the spinal cord, brain and optic nerves, characterized by disseminated areas of demyelination and glial scar formation. It may involve the optic nerves as acute or as chronic optic neuritis, either in the retrobulbar form or with papillitis.

In acute retrobulbar neuritis, usually one eye is involved at a time. The onset is rapid, over a period of one to five

days, frequently with the appearance of a large central scotoma and severe reduction in vision. For a few days prior to the visual loss there is commonly an aching pain about the eye and a sharper pain when the eye is turned. There is a remarkable tendency to spontaneous recovery within four to eight weeks. The optic discs appear normal at this stage. This course of events is not specific for multiple sclerosis but is typical of acute retrobulbar neuritis, whatever its cause. Following an episode of acute retrobulbar neuritis, the chances of return to normal or near normal vision are about 50 per cent. The outlook is better than this when the episodes occur early in the course of multiple sclerosis, not so favorable when they occur later. Recurrences in an eye previously affected are uncommon, estimates ranging up to 10 to 15 per cent, and are likely to be less severe than the first attack. When the lesion is located close to the globe, papillitis appears, manifested as a swelling of the nerve head. Its frequency is only one tenth that of the retrobulbar variety with its flat discs. Recovery when the nerve head is edematous is likely to be slower than when it has a normal appearance.

Chronic retrobulbar neuritis is encountered rarely in established multiple sclerosis. In contradistinction to the acute form, this form is frequently bilateral. Without obvious episodic exacerbations, vision slowly deteriorates. The examiner finds central scotomas and pallor of the optic discs. Recovery is not to be expected, but spontaneous improvement is experienced by some patients even after a lapse of several years.

Congruous homonymous defects are rarely, if ever, encountered in the visual fields in multiple sclerosis, in spite of the pathologist's frequent finding of plaques along the optic radiations.

The relationship of multiple sclerosis to optic neuritis has been under discussion for a long time. Reported series of cases indicate that in a group of patients who have multiple sclerosis, the optic nerves will be affected at some time in 30 to 50 per cent. In about one half of these, involvement of the optic nerves will be the first evidence of the disease, preceding other symptoms by periods ranging from one to fifteen years.[3,5,10,11]

When a patient between the ages of 20 and 45 years exhibits unilateral acute retrobulbar neuritis without any other neurologic manifestations, the chances are 50 per cent that other evidence of multiple sclerosis will appear within fifteen years. Among patients less than 20 or more than 45 years of age, this implication does not hold.[9]

Multiple sclerosis appears to be distributed randomly among all races, nationalities, social levels and occupational groups. It occurs in both sexes and appears to be selective only in the age factor, since mainly young adults are affected. Undoubtedly significant, but unexplained, are its relatively high incidence and death rate in Canada and in northern regions of the United States, and its low incidence in the South.[1]

Pregnancy has no influence on the occurrence or the course of the disease.[4] That excessive fatigue and chilling may intensify the symptoms and induce exacerbations is the clinical impression of a number of investigators, but it lacks substantiating evidence.

The etiology of multiple sclerosis is unknown, and there is no treatment of demonstrated efficacy.[6,7] The same holds for its involvement of the optic nerves. Clinicians who have claimed cures or benefit from one form of treatment or another usually have failed to take into account the natural course of the disease and its unpredictable spontaneous fluctuations. To be recommended are any measures that hold promise of improving the patient's general health, including

adequate rest. Vitamins may be prescribed, preferably B complex. Nicotinic acid may have some psychotherapeutic value. Cortisone and corticotropin (ACTH) are worthless in this disorder, and their prolonged use is hazardous.

The indiscriminate diagnosis of multiple sclerosis is to be decried. Diagnosis cannot be made on the basis of any single sign, such as optic neuritis, nor is it the business of the ophthalmologist to make such a diagnosis. The senseless comment, "You may have multiple sclerosis," may condemn a patient to years of needless anxiety. A wise and considerate neurologist, after a thorough examination, is in a better position to discuss the diagnosis and prognosis than is the ophthalmologist.

Multiple sclerosis is not inevitably the grim disease it has been thought to be. Recent studies indicate that the average duration of the disease is twenty-seven years, that by and large it does not greatly shorten the span of life, and that the majority of patients have remissions.[2] Although the course of the disease in an individual case is unpredictable, the physician may, without deceiving the patient, present an encouraging outlook.

OPTIC NEUROMYELITIS

Neuromyelitis optica (Devic's disease) is a rare syndrome in which bilateral acute optic neuritis is associated with acute inflammation of the spinal cord.

The syndrome occurs at any age, from 6 to 60 years. Prodromal signs of headache, sore throat, fever and malaise, preceding the major symptoms by several days or more, suggest that the etiologic basis is an infection, although no organism has been demonstrated.

The visual loss is rapid and intense, with blindness or near blindness, first in one eye and a few days later in the other. Within a few weeks, either before or after blindness, signs of severe involvement of the spinal cord appear, with ascending paralysis and sensory disturbances. The initial lesion involves the optic nerves or the spinal cord with about equal frequency. The patient may die within a month or so, may survive for several years with one or more remissions, or may even recover. In cases in which optic neuritis is the first major incident, the prognosis seems to be rather better than in those in which myelitis develops as the first major event. Cases in which severe bilateral optic neuritis occurs, without other involvement of the nervous system, may be an incomplete form of neuromyelitis optica. The optic neuritis, or the myelitis, may recur.[8]

Most writers agree that neuromyelitis optica is a real disease entity and not a form of multiple sclerosis. There is no effective treatment.

PROGRESSIVE SUBCORTICAL ENCEPHALOPATHY

Schilder's disease (encephalitis periaxialis diffusa) is a malady of children and young adults characterized by loss of vision, spastic paralysis, mental deterioration and death in a few months to a year. In a majority of cases the optic discs are edematous. The recognition of Schilder's disease can only be suspected during life from the neurologic manifestations and the failing mentality. The positive diagnosis rests with the pathologist.

POSTINFECTIOUS ENCEPHALITIS

This group includes the cases of involvement of the brain and optic nerves following viral infections, as after measles, mumps, chickenpox and vaccination against smallpox. Differential diagnosis is dependent on the history.

Encephalitis occurs in a fraction of 1 per cent of cases of measles, coming on a few days after the rash and entail-

ing a mortality rate of about 10 per cent. The optic nerves may exhibit evidence of papilledema, papillitis, or retrobulbar neuritis. Recovery of vision is excellent.

Encephalitis is a rare complication of mumps. One of its signs is optic or retrobulbar neuritis coming on during or within a few weeks after the involvement of the salivary glands. While other neurologic symptoms generally tend to subside, the outlook for involvement of the optic nerve is less favorable. In one reported series only one half of the patients recovered normal vision, and several remained completely blind.

Encephalitis complicating chickenpox is a rare cause of optic neuritis, which may be severe. The tendency to recovery is good.

Encephalitis may follow vaccination against smallpox, coming on two to twenty-four days after vaccination. The course is rapid and stormy, lasting only one or two weeks and terminating, in half the cases, in recovery and, in the other half, in death. The optic nerves may be involved through optic atrophy, or through optic neuritis with transient blindness and secondary atrophy. Even with intense involvement of the optic nerves there may be no other clinical manifestations of encephalitis.

That this complication does not arise in infants less than one year of age is one reason for the desirability of vaccinating babies against smallpox during the first year of life.

The so-called demyelinating diseases share the one characteristic of loss of myelin sheaths. In other respects, especially in their clinical manifestations, it is obvious that they differ widely, and form a loose, heterogeneous group.

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VIII

PATHOLOGY OF THE DEMYELINATING DISEASES

LORENZ E. ZIMMERMAN, M.D.

MULTIPLE sclerosis, neuromyelitis optica (Devic's disease), diffuse sclerosis (Schilder's disease), and acute disseminated encephalomyelitis (postvaccination or postinfection) are disorders of unproved etiology, uncertain pathogenesis, and unestablished relationship. They are generally considered together because certain histopathologic features which they have in common suggest a fundamental relationship to many observers. It should be emphasized, however, that in typical cases there are unmistakable anatomic differences among these diseases. This fact, together with important clinical differences characteristic of each, has made their apparent relationship questionable.

The essential process which keeps them together as a group is demyelination. Demyelination occurs in a great many conditions and can be produced experimentally by a variety of techniques. In this group of disorders, however, the demyelinating process seems to occur early and is often out of proportion to the damage observed in axons, nerve cells and supporting structures. Certain details of this process seem to be similar throughout the group. Associated with the early degeneration of myelin, there is also degeneration of oligodendrocytes. Microglia are mobilized early. The damaged myelin is phagocytized and converted into fat (fig. 1). Later there is an astrocytic response eventuating in the characteristic glial sclerosis (fig. 2).

TABLE I

COMPARATIVE PATHOLOGIC ANATOMY OF THE DEMYELINATING DISEASES

	CHARACTERISTIC LESION	TISSUES INVOLVED	DIFFERENTIAL HISTOPATHOLOGIC FEATURES
Multiple Sclerosis	multiple irregular patches, 1 mm. to more than 5 cm. in diameter	white matter of brain, spinal cord, optic nerves	minimal necrosis and axonal degeneration; mild mesodermal and microglial reaction
Acute Disseminated Encephalomyelitis	widespread patches seldom larger than 2 to 3 mm.	gray and white matter of entire CNS including optic nerves	striking perivenous distribution and mesodermal reaction
Neuromyelitis Optica	massive degeneration	gray and white matter of spinal cord, optic nerves	marked necrosis of nerve fibers and intense microglial response
Diffuse Sclerosis	massive degeneration	hemispherical white matter, optic nerves	varying degrees of necrosis and tendency to cyst formation

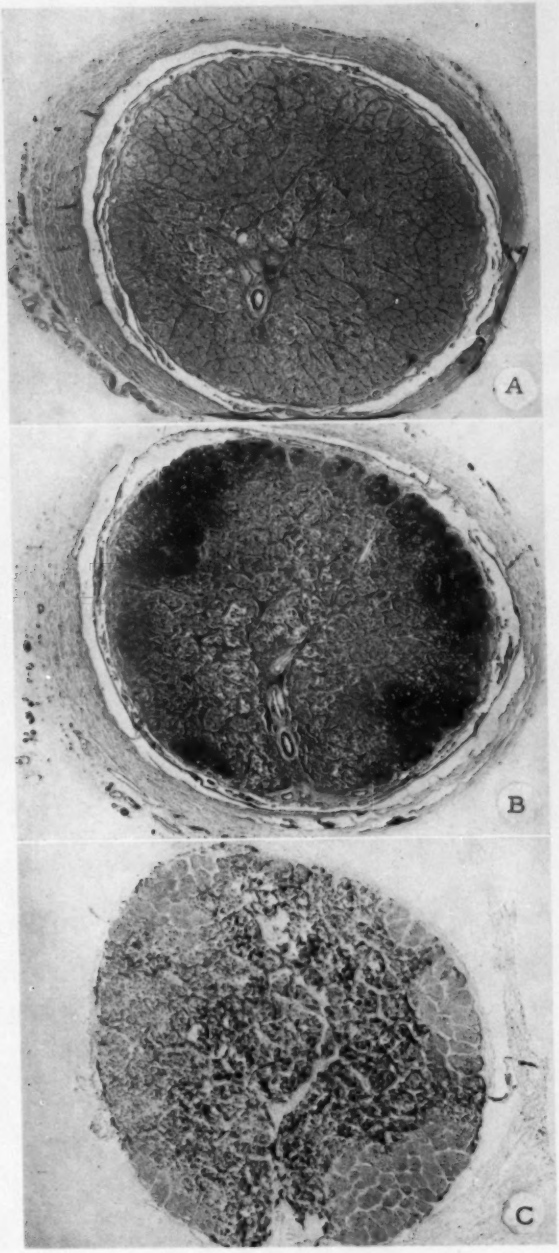

FIG. 1—AFIP Acc. 300459. (A) Hematoxylin-eosin, (B) myelin sheath, and (C) oil red O stains of adjacent sections of optic nerve in neuromyelitis optica. Only a few nerve bundles about the periphery remain intact. In the central area of severe damage, much neutral fat demonstrable by the oil red O stain has been liberated. (All, × 19)

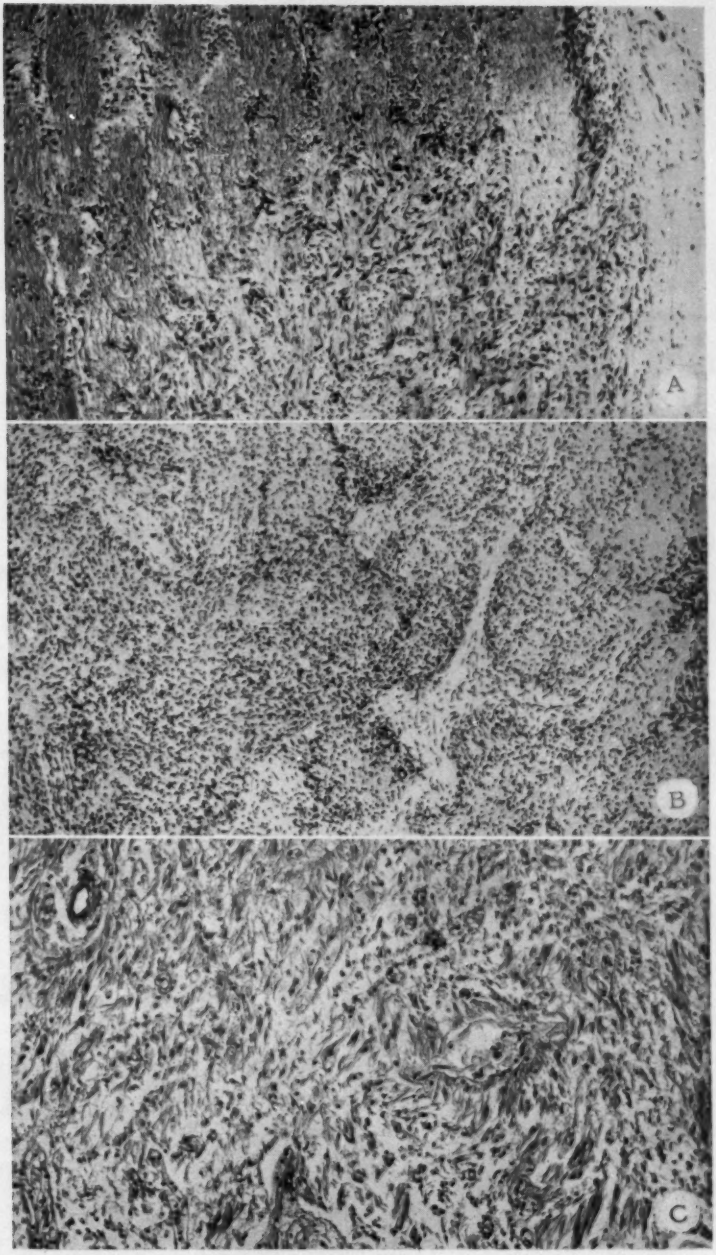

FIG. 2—Evolution of histologic changes in neuromyelitis optica. (A) AFIP Acc. 300459. The demyelination of optic nerve fibers is seen along the advancing margin of an early lesion. Myelin sheaths are still intact along the upper and left margins of the field. (Myelin sheath stain, × 75) (B) AFIP Acc. 219944. The lesion at its height is extremely cellular. (H & E, × 70) (C) AFIP Acc. 303115. Finally the destroyed optic nerve tissue is replaced by fibrous astrocytes. (H & E, × 130)

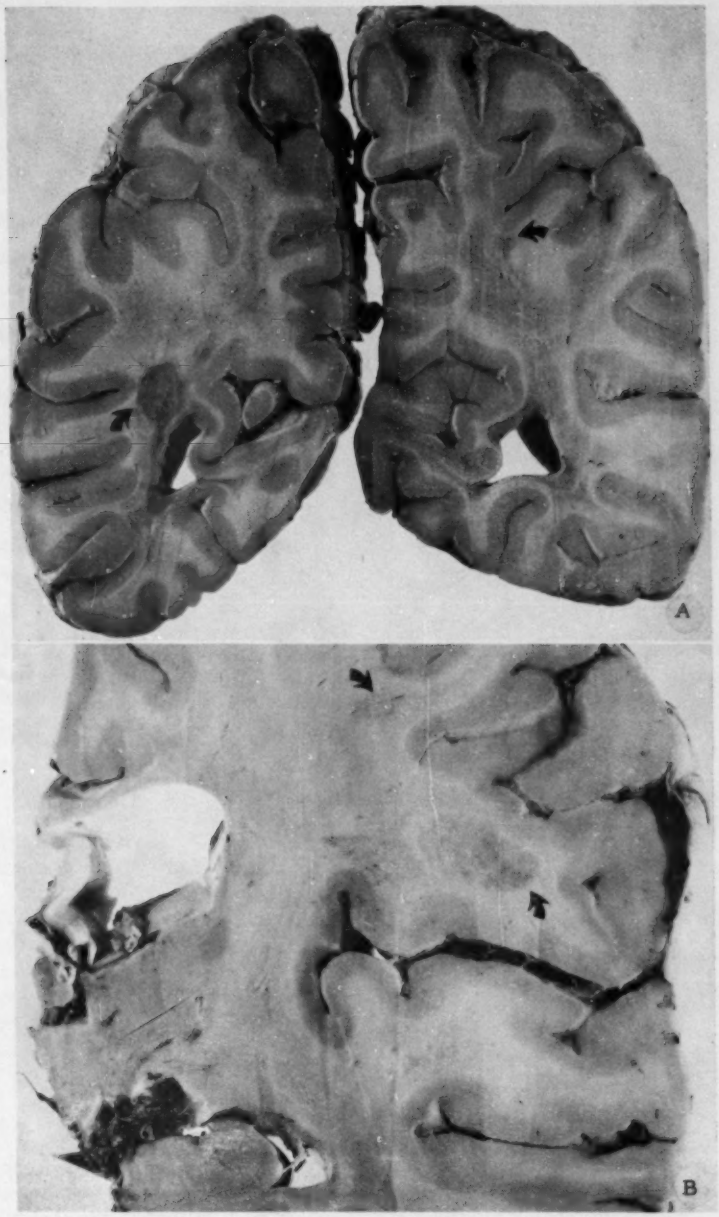

FIG. 3—(A) AFIP Acc. 547859. **Extensive involvement of periventricular white matter** and formation of discrete plaques (arrows) in chronic multiple sclerosis. (B) AFIP Acc. 550194. Multiple plaques in subcortical white matter (arrows) in another case of chronic multiple sclerosis.

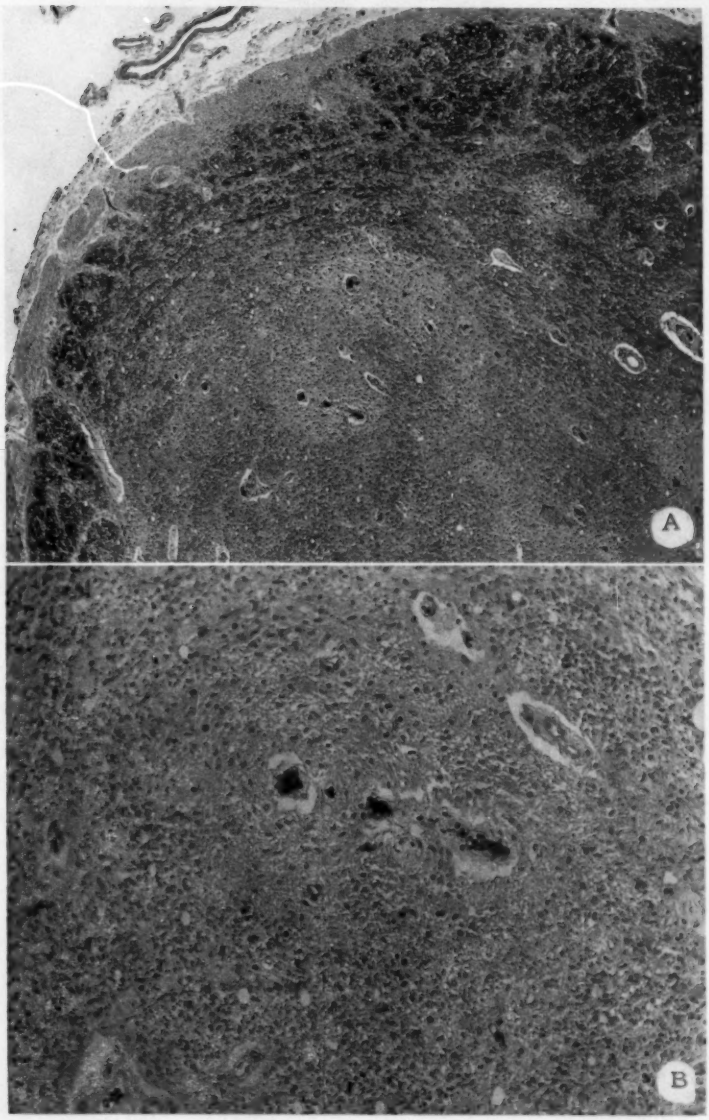

FIG. 4—AFIP Acc. 543856. There is a distinct perivenous pattern of demyelination in the optic nerve of this patient, who died of acute multiple sclerosis. (B) is an enlargement of the vein seen in the lower central field of (A). (Myelin sheath stain; (A) × 45; (B) × 160)

FIG. 5—AFIP Acc. 543856. Extensive softening of the periventricular white matter in acute multiple sclerosis. Same case as that illustrated in figure 4.

It is my main task, however, to point out some of the distinguishing antomical features of these diseases (table I).

In multiple sclerosis there are widely scattered, irregular lesions of varying ages and measuring from 1 mm. to more than 5 cm. in diameter (fig. 3). They occur characteristically in the white matter and may show a perivenous distribution (fig. 4). Extensive periventricular involvement is typical (fig. 5) and optic nerve lesions are frequent (fig. 6). The disparity between destruction of myelin sheaths and preservation of axis cylinders is greater in multiple sclerosis than in the other demyelinating diseases (fig. 7).

In acute disseminated encephalomyelitis, the lesions are even more widespread, involving the gray matter as well as the white. They are smaller, not more than a few millimeters in diameter (fig. 8), and show the most striking perivenous distribution (fig. 9). There is an especially intense inflammatory response, with exudation of lymphocytes and plasma cells.

Neuromyelitis optica, considered by some as a form of acute multiple sclerosis, is characterized by more massive lesions involving the optic nerves and spinal cord (fig. 10). There is a greater destruction of axis cylinders and more involvement of gray matter than in multiple sclerosis. The microglial response is especially intense.

Diffuse sclerosis is also characterized by more massive lesions, but these involve predominantly, or exclusively, the hemispherical white matter (fig. 11). The optic nerves are often involved. Destruction of axons is relatively great.

Adams and Kubik (see Bibliography) have called attention to their observation that in addition to demyelination, there are two other morphologic changes common to these diseases: perivenous dis-

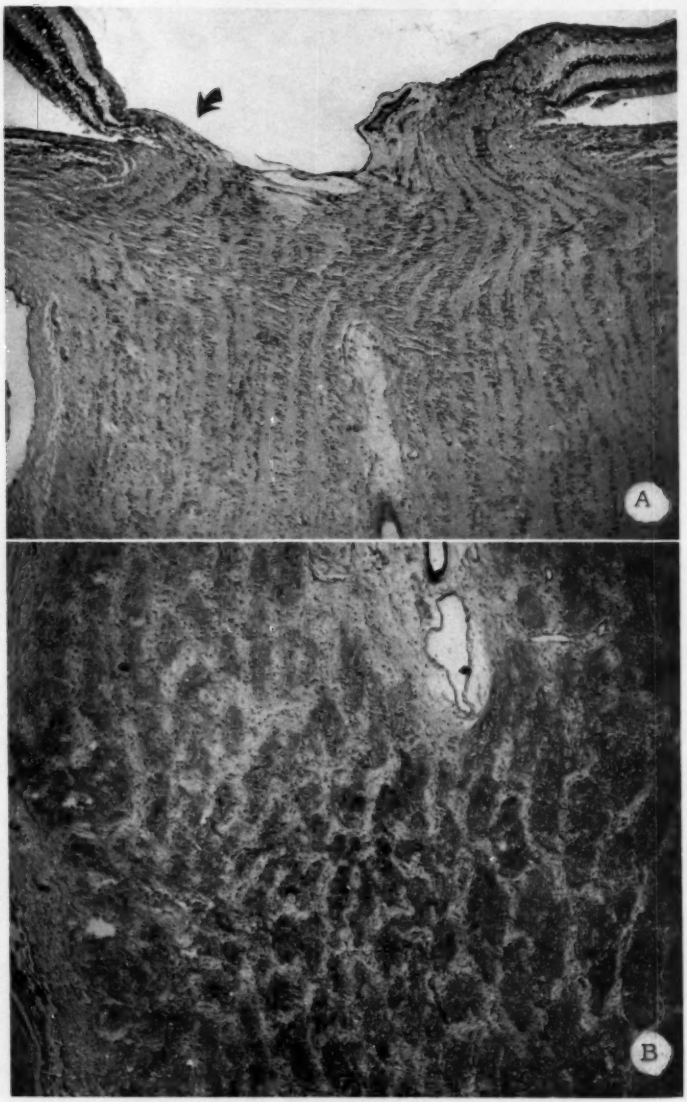

FIG. 6—AFIP Acc. 490261. (A) Atrophy of temporal half (arrow) of optic nerve head in multiple sclerosis. (H & E, × 48) (B) Myelin sheath stain of optic nerve just posterior to field shown in (A). There is marked atrophy and demyelination on the temporal (left) side of the optic nerve. Central retinal vessels are seen at top of field. (× 48) (Sections contributed by Dr. Jonas Friedenwald.)

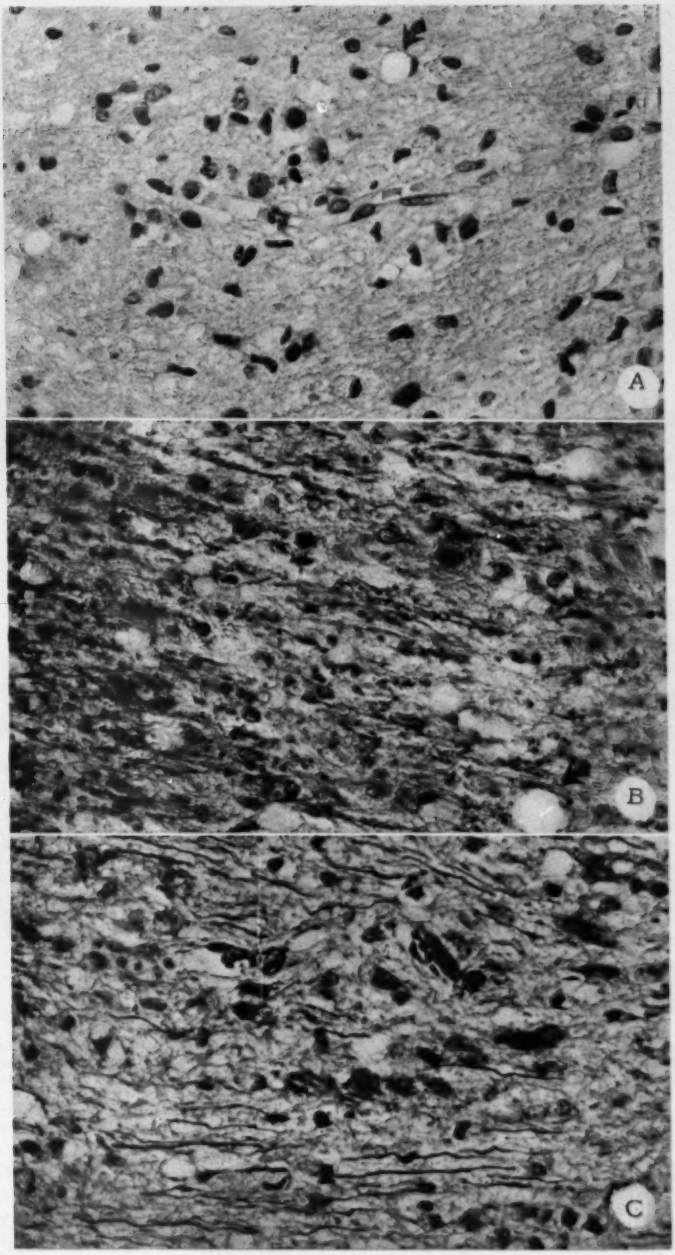

FIG. 7—AFIP Acc. 543856. Adjacent sections of a lesion in the optic chiasm from the same case of acute multiple sclerosis shown in figures 4 and 5. There is mobilization of glial and inflammatory cells, some of which have phagocytized large quantities of fat liberated by the destruction of myelin sheaths. These appear as signet ring cells (arrows). There is much less complete destruction of axis cylinders (C) than of myelin sheaths (B). (A) H & E; (B) myelin sheath stain; (C) axon stain; all, × 395.

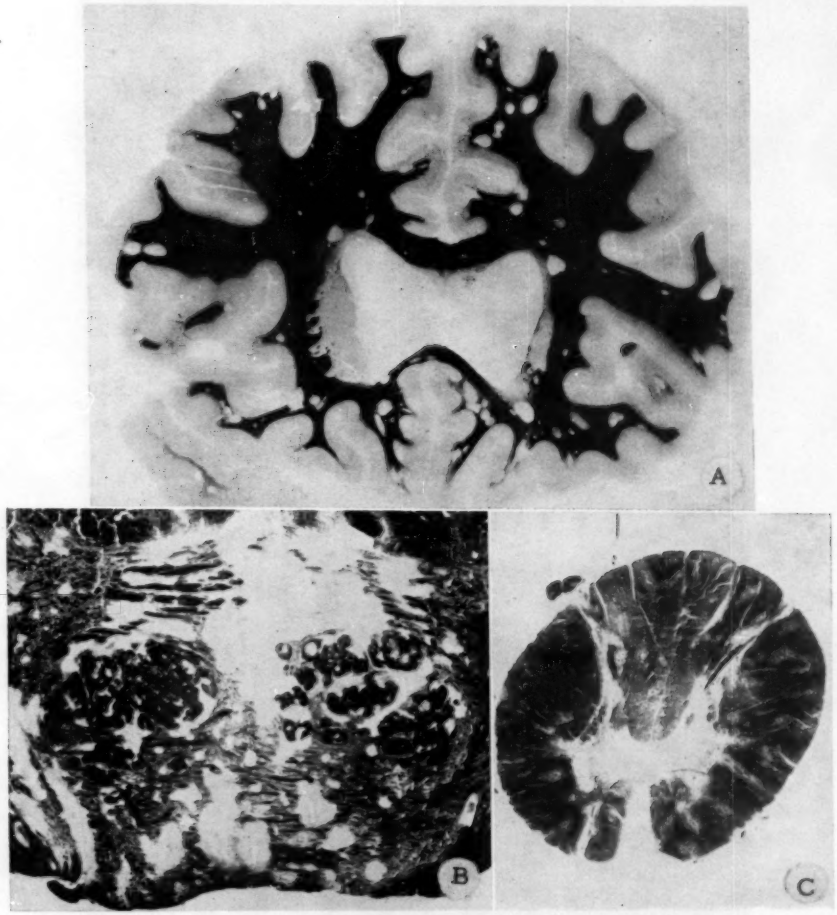

FIG. 8—AFIP Acc. 312166. Widespread patches having a distinct perivenous distribution are characteristic of the disseminated encephalomyeltides that follow acute exanthematous diseases or vaccination. Myelin sheath stains of cerebrum (A), pons (B), and upper cervical cord (C). (All photomicrographs are from the Scholz collection.)

tribution of lesions and perivascular exudation of inflammatory cells. Because of these pathologic similarities, it seems reasonable to expect a similar pathogenesis. The pathologic changes in these disorders are unlike those of known infectious and metabolic diseases of the brain. At the present time the essential pathologic features seem to have more in common with those of experimental allergic encephalomyelitis, and for this reason the morbid anatomy of the demyelinating diseases favors the allergic theory (Adams and Kubik).

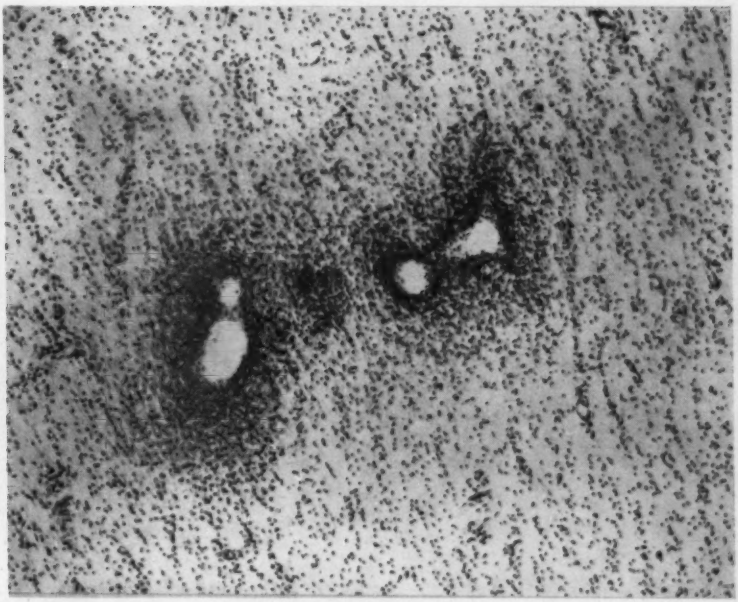

FIG. 9—AFIP Acc. 312166. An intense perivascular infiltration by lymphocytes and plasma cells is especially characteristic of the postexanthematous encephalomyelitides. (Photomicrograph from the Scholz collection of a case that followed smallpox.) (Nissl stain; × 50)

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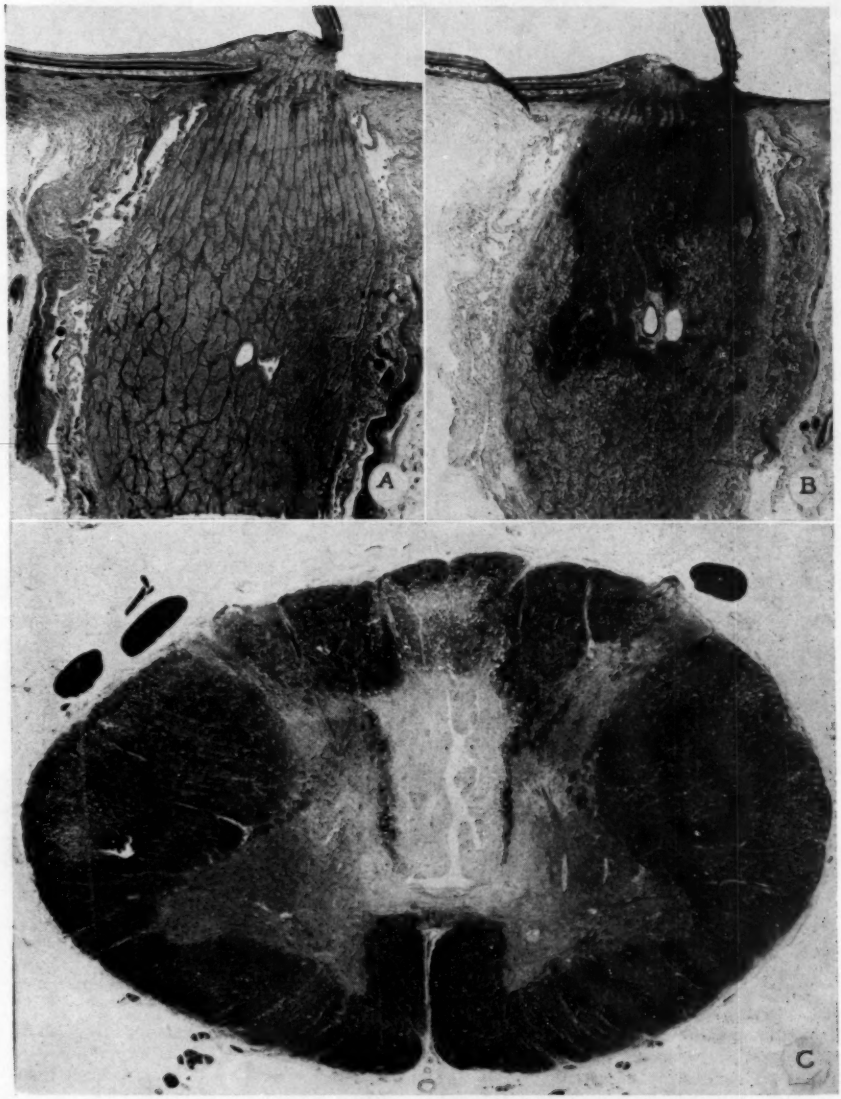

FIG. 10—AFIP Acc. 300459. Massive involvement of optic nerves and spinal cord in neuromyelitis optica. (A) and (B) are hematoxylin-eosin and myelin sheath stains, respectively, of adjacent sections of the optic nerve. The areas of simple demyelination appear paler than the normal nerve in both illustrations. The somewhat darker staining to the temporal (right) side of the central vessels within the area of demyelination is due to an intensely cellular infiltrate. (× 15) (C) Myelin sheath stain of lower cervical cord. The extremely pale staining in the rectangular area just posterior to the gray commissure (in the posterior funiculi) is due to massive necrosis and total demyelination. At other levels there was almost total transverse myelitis. (× 11)

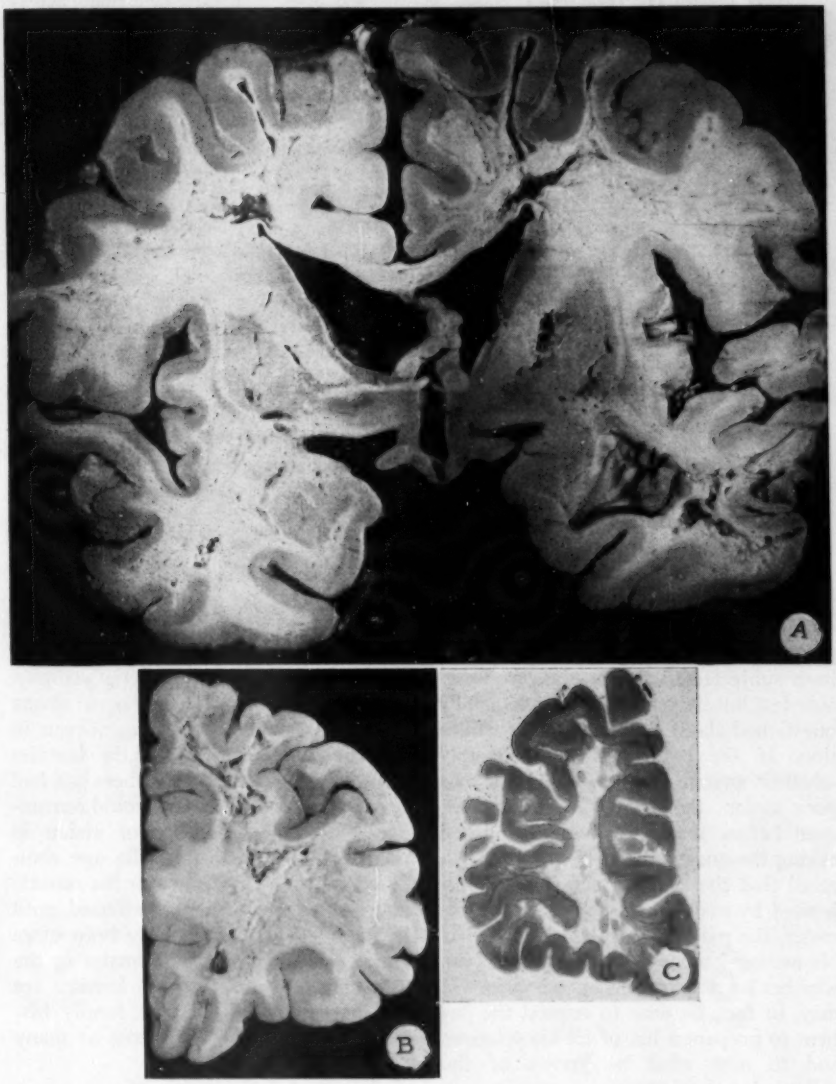

FIG. 11—AFIP Acc. 631436. There is diffuse softening of the hemispherical white matter bilaterally in this case of Schilder's disease. Characteristically, the process begins in the occipital lobes (B and C) where the optic radiations are included in the destroyed white matter.

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IX

HEREDITARY AFFECTIONS

FRANK D. CARROLL, M.D.

IN my experience, one of the most frequently overlooked known causes of optic neuritis is hereditary disease. Each year I see several patients who have been subjected to almost every conceivable test but never have been adequately questioned about any familial eye condition. If the patient is asked simply whether anyone else in his family has poor vision, the answer is usually no, even before the physician has finished asking the question. But if it is borne in mind that the disease is frequently inherited by males through unaffected females, the patient may then be asked if his mother had any brothers; and if so, whether or not they had good vision. It may, in fact, be wise to request the patient to prepare a list of all his relatives and to note what he knows of the vision of each of them.

Hereditary optic atrophy may be congenital, and in some cases there may be other involvement of the nervous system, including mental deficiency.[1-7] The hereditary factor in some of the congenital cases appears to be dominant, but almost any type of inheritance is possible. In Leber's disease, which probably differs from congenital optic atrophy, the onset of poor vision may occur at any age, from infancy to old age, even in the same family. In one of the families under my care, several members had had poor vision as long as they could remember, others first noted poor vision in their twenties (which is the age commonly regarded as usual for the onset), and one member was not affected until 57 years of age. Males have been more frequently affected than females in the various reported series, but females are also affected, and in some family histories there have been almost as many females as males.

The symptoms, signs, and early course of hereditary optic atrophy are the same as those of retrobulbar neuritis or papillitis from other causes. The second eye is usually involved within a

few days or weeks following involvement of the first eye, but an interval of as long as 18 months has been recorded. The disc in the early stage may appear normal or may be elevated several diopters; later, there is marked pallor of the temporal part, or even of the entire disc. Visual field examination usually reveals the presence of central or centrocecal scotomas. These are often very dense and frequently break through to the periphery in the upper nasal quadrant. There is great variability in the degree of final vision: in the same family, some members may have vision as good as 20/30 to 20/50, while the majority will have 20/200 or less. Total blindness is very rare. Usually the vision becomes stationary within a few months.

There are doubtless a number of cases of severe bilateral optic neuritis, especially those occurring in males, of undetermined etiology that could be placed in this category if more were known of the heredity. It is probably safe to advise the male patient that his offspring will not be affected since transmission is usually through the unaffected females.[6]

There is no treatment of value, but some cases have apparently improved spontaneously.

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X

CIRCULATORY DISORDERS

C. WILBUR RUCKER, M.D.

DISEASE of the nutrient arteries of the optic nerves is an occasional cause of loss of vision. The affections include senile atherosclerosis, arterial hypertension, and several varieties of inflammation of the walls of the arteries.

ATHEROSCLEROSIS

Senile atherosclerosis may cause *closure of the central retinal artery* through formation of an atheromatous plaque, which encroaches on the lumen of the artery and leads to formation of a thrombus. This may induce a contraction of the walls of the artery, to be followed later by relaxation. The ophthalmoscopic picture is well known: extensive ischemic edema of the retina, a red spot at the fovea, and visible segmentation of blood in the retinal vessels. Within a day or so the retinal vessels may widen and the flow of blood through them be restored; the whiteness of the retina fades away over a period of about two weeks; later the nerve head becomes pale and the retinal vessels become attenuated.

Atherosclerosis also may cause *pseudoglaucoma* (soft glaucoma)[3,5,7] by obstructing some of the small arteries which supply the optic nerve in the region of the lamina cribrosa. The resulting ischemic degeneration and disintegration of nerve fibers without proliferative gliosis lead to displacement backward of the lamina cribrosa, and the ophthalmoscopic appearance of pallor and excavation of the optic nerve head. The defects in the visual fields are largely arcuate, although some tend to be altitudinal. They progress slowly, but seldom as far as complete blindness. Roentgenograms of the nerve head may disclose calcification of the internal carotid arteries, but the relationship is negligible.

Abnormally placed vessels and fusiform aneurysm deserve consideration in the differential diagnosis.

A diagnosis of pseudoglaucoma is to be made cautiously, for in several instances reported in the literature the correct diagnosis eventually proved to be brain tumor, and in others the disease turned out to be true glaucoma. Absence of hemianoptic defects in the visual fields should aid in the differentiation of pseudoglaucoma from brain tumor. Repeated observations of the intraocular pressure, and perhaps tonography or provocative tests, should differentiate it from glaucoma.

Treatment at present is ineffective. Filtering operations performed to lower the intraocular pressure have been found to be without benefit.

HYPERTENSIVE DISEASE

Hypertensive disease may lead to sclerosis of the arterioles; if the process is intense enough, it may lead to their closure. The central retinal artery itself, or one of its branches, may be occluded, resulting in atrophy, either of the entire optic disc or of one of its sectors. In malignant hypertension, the optic nerve heads become edematous, a condition that can be differentiated from the papilledema of brain tumor by the presence of hypertensive sclerosis and focal constrictions in the retinal arteri-

oles and of hemorrhages and exudates in the retina. When retinitis is absent, differentiation may be difficult.

ARTERITIS OF UNKNOWN ORIGIN

Inflammatory diseases, of which little is known at the present time, may affect the nutrient vessels of the optic nerve or nerve head, resulting in what may be termed "ischemic optic neuritis." It seems to be most frequent in patients of middle age rather than in the elderly, as is temporal arteritis, and it is not accompanied by heightened sedimentation rate or other evidence of generalized infection. Its course is not as favorable as is that of the usual optic neuritis.

THROMBOSIS OF THE INTERNAL CAROTID ARTERY

Spontaneous thrombosis of the internal carotid artery is an uncommon disorder that accounts for an occasional case of loss of vision.[6,8] Although it leads to no recognized, regular sequence of symptoms, it should be suspected on the basis of a history of transient obscurations of vision of one eye and episodes of contralateral hemiparesis and hemianesthesia. After several months the disturbed eye may suddenly become completely blind as a result of closure of the central retinal artery, or there may be a contralateral hemianopsia as a result of cerebral infarction. The ophthalmodynamometer will demonstrate a lowered pressure in the central retinal artery on the side of the thrombosed internal carotid artery.

PERIARTERITIS NODOSA

Periarteritis nodosa is such a rare cause of optic neuritis that it is mentioned here only for the sake of completeness. While there seems to be no sharp cleavage between it and temporal arteritis from the histopathologic standpoint, the clinical courses of these two disorders are vastly different. In periarteritis nodosa the retinal arterioles exhibit hypertensive changes, and the choroid, if it is involved, contains white patches that resemble those of acute choroiditis, with a tendency to rapid regression.[4]

TEMPORAL ARTERITIS

Some instances of sudden and tragic blindness are due to temporal arteritis,[1,2] a disease in which there is inflammation in the walls of arteries of various parts of the body, especially of those about the head. It is a disease of elderly persons, occurring with rare exceptions only after the age of 60 years. When arteries of the anterior portion of the optic nerve are involved, as they are in nearly half the cases, loss of vision ensues. Furthermore, when one eye is affected, the chances are about even that in the next few days or weeks the other eye will be affected also. Vision, once lost, seldom returns. Ophthalmoscopic examination may disclose a pale swelling of the optic disc characteristic of ischemic optic neuritis, or there may be an associated incomplete closure of the central retinal artery, or the nerve head may appear normal. Within a week or two the nerve head becomes pale.

There are other symptoms besides those about the eyes, though none as frightening: the temporal arteries become painful, tender and swollen as a result of inflammation and thrombosis; clinical features include anorexia, loss of weight, severe headache, leukocytosis, fever and a high sedimentation rate.

Temporal arteritis, when it impairs vision, becomes a medical emergency, for when one eye is affected there is grave danger that the other will be affected also, and the end result may be complete blindness. At present the most effective therapeutic agent is cortisone

administered systemically, not dropped in the eye. It seems to control the inflammatory reaction, for after its administration is begun further loss of vision seldom ensues and the second eye almost never becomes affected.

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XI

MECHANICAL TRAUMA

FRANK B. WALSH, M.D.

INJURIES to the optic nerve are here described according to the following classification:

Direct Injuries
- Avulsion of the optic nerve
- Division of the nerve, partial or complete
- Direct trauma without division associated with pressure or fracture

Indirect Injuries to the Optic Nerve

Unusual Injuries to the Optic Nerve

DIRECT INJURIES

Avulsion of the Optic Nerve

Usually this injury is the result of a blunt instrument being shoved forcibly into the orbit. The optic nerve may be jerked backward and pulled from the eyeball, or the eyeball may be shoved sharply forward when the nerve is jerked from its attachment. In most instances of avulsion, the nerve is pulled out of the globe as, for example, when the horn of a bull has entered the orbit. The gouging effect of striking the lateral aspect of the orbit on a protuberance may shove the eye forward, avulsing the nerve without visible evidence of any object having been inserted into the orbit. The optic nerve may be avulsed as a result of a blow on the eye as, for example, a blow with a fist. The optic nerve is forced out of the globe in the manner that a cork is forced out of a bottle by striking the butt of the bottle on a wall. In such an instance there may be concomitant multiple ruptures of the choroid. Avulsion may be the result of birth injury. It may result from a bullet wound. We have observed avulsion of one optic nerve and total atrophy of the other nerve as a result of a bullet wound which traversed the orbit. Avulsion may be complete or incomplete. In the for-

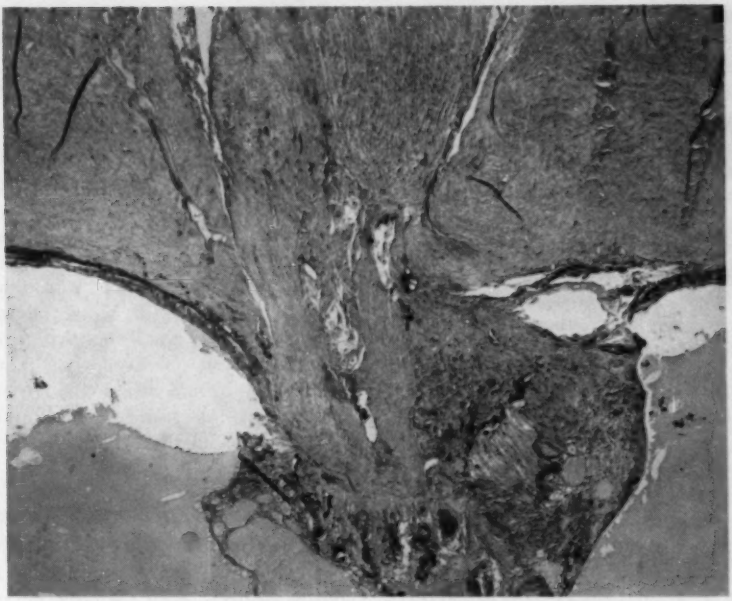

FIG. 1—Cutting injury of the optic nerve.

mer instance all sight is lost. When incomplete, the visual defect is likely to correspond to the area of separation, and in such cases visual acuity is invariably defective. With avulsion, the fundus picture varies within wide limits. Usually immediately after the accident has occurred there is blood in the eye and it is impossible to make the diagnosis. By the time the blood has been absorbed, there is likely to be much fibrous tissue in the posterior aspect of the eye so that the diagnosis must be inferred. When avulsion has been complete, it is often impossible to recognize retinal vessels in the fundus. Incomplete avulsion may result in the development of a pigmented ring about the optic disc, and it has been suggested that the pigment is derived from hemorrhage which has occurred into the optic nerve sheaths. There is no effective treatment.

Division of the Optic Nerve

The optic nerve may be severed completely or incompletely. If division is complete, the site of injury in some instances may be inferred from the symptomatology. When such a division occurs close to the eyeball, the central retinal vessels are severed. There is immediate blindness of the injured eye. The oph-

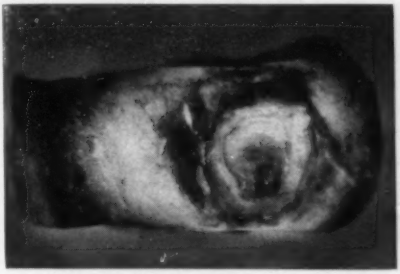

FIG. 2—Metallic foreign body in optic nerve.

thalmoscope reveals a picture of obstruction of the central retinal artery. Immediately the optic disc becomes white, the retina becomes gray, the retinal vessels are narrowed, and there is development of a cherry-red spot at the macula. Section of the optic nerve rather far forward may be elective when a section of the nerve is removed for tumor. In such instances the optic fundus picture is that which is seen as a result of retinitis pigmentosa. It is also seen in experimental animals when the ciliary arteries have been divided.

Section of the nerve may originate as a result of injury through the posterior orbit. When the nerve is divided posterior to the entrance of the central retinal vessels, there is, of course, immediate total loss of vision. The ophthalmoscopic appearance of the fundus is at first normal. Some degree of pallor and narrowing of the retinal vessels appears in three weeks or less in such cases. Pallor of the disc develops according to the site of section; an intracranial division will produce pallor less rapidly than an orbital division. Injury to the nerve in the canal is thought to result in change in the appearance of the optic fundus in approximately three weeks.

Intracranial division of the nerve occurs as a result of accident in some instances. Rather often there is an associated injury to the chiasm, and such an association is diagnosed on the basis of defects in the visual fields.

It would be anticipated that fracture of the optic canal might be a frequent explanation for injury and division of the optic nerve. The optic canal is particularly resistant to fracture, according to many observers, but such fracture does occur. Fracture of the canal, with a splinter of bone lodging in the optic nerve, has been observed, and in one instance removal of the splinter failed to produce any vision in the injured eye. Injury in the region of the optic canal is further considered under "indirect injury." Delayed onset of visual loss after trauma should suggest fracture of the canal as a possibility.

Division of the nerve, partial or complete, may be associated with intracranial damage, particularly in stab wounds. Stab wounds of the orbit are likely to involve the cavernous sinus as a result of a knife or stiletto passing through the superior orbital fissure into the cavernous sinus. As a result, ophthalmoplegia is rather often observed. In other instances an orbital hematoma resulting from an orbital wound may account for loss of vision in the eye on the injured side.

Direct Trauma Without Division and Associated with Pressure or Fracture

Up to this point descriptions have concerned division of the optic nerve as, for example, by knife, icepick and bullet and by avulsion. Loss of function has in such cases been due to actual interruption of the nerve. In many instances trauma produces loss of function from swelling of tissue, pressure of a bone fragment, or interference with blood supply. In some such cases the trauma is indirect, as will be explained subsequently under a separate heading. As regards direct trauma to the optic nerve, it may be quite impossible to state whether or not the nerve has been severed if the loss of vision follows immediately after the injury. If there is some recovery of vision in such an instance, it may be concluded that the nerve has been partially severed or that the injury to the nerve has been indirect, probably through interference with blood supply. When the loss of vision is delayed following an injury, it is positive proof that the nerve has not been severed; in such instances of loss of vision delayed for a day or two after the accident, the prognosis for return of vision is reason-

ably good. When loss of vision is delayed for weeks after an injury has occurred, callus may be pressing on the optic nerve in the optic canal.

In rare instances, visual acuity which has been reduced or absent may improve weeks after injury to the optic nerves. We recently observed an individual who was unable to perceive light with either eye for one week. During the second week, perception of light appeared in one eye. Within a second fortnight visual acuity was 15/200 for each eye.

INDIRECT INJURIES TO THE OPTIC NERVE

Trauma to the region of the external angular process or to the forehead — rarely, injuries to the posterior portion of the head — may produce an immediate loss of vision in the eye of the injured side of the head. Such loss of vision varies within wide limits; rather often it is profound. Often there is no evidence of fracture, and in some instances the injury may have seemed too trivial to account for the loss of vision. In many such cases of indirect injury to the optic nerve, there is a definite pattern of visual loss and recovery of vision.

Indirect injury may occur with or without a fracture of the region of impact or remote from it. Consciousness may or may not be lost. The loss of vision occurs immediately. Improvement may commence within three or four days after the injury has occurred, and complete loss of vision does not necessarily indicate a bad prognosis. After the improvement of vision commences, it continues for three or four weeks until it has attained its maximum. Rather often, the fundus appearance remains normal early after the accident, although in some instances retinal hemorrhages are present. There may be swelling of the optic disc a few days after injury. About three weeks after the injury has occurred, there is development of pallor of the optic disc. This time interval suggests that injury to the optic nerve has been in the optic canal. Interference with blood supply may be the responsible factor. It has been suggested that injury results either in thrombosis of small vessels supplying the nerve or in intraneural hemorrhage. This is the same explanation that is offered for so-called rupture of the chiasm, in which it has been shown that there is not an actual rupture of fibers. Indirect injury must be differentiated from division of the nerve and from injury in which pressure accounts for immediate loss of vision. Delay in the onset of loss of vision after an accident indicates intactness of the nerve and suggests a physiological block from which recovery may be anticipated. In indirect injuries, the field defects are usually central (or paracentral) scotomas or sector defects. In other cases there is loss of the inferior half of the field of the affected eye.

UNUSUAL INJURIES TO THE OPTIC NERVES

Electrical Current Injuries and Lightning Strokes

Usually electrical injuries (electric current and lightning) do damage by burning. Actually the body tissues, excepting the nerves, are poor conductors of electricity, and death as a result of such accidents results from shock in most instances. Optic atrophy occurs as a result of electric-current injury or lightning stroke.

Injuries Associated with Operations on the Nose and Lacrimal Sac

The operation reported as intranasal ethmoidectomy has been followed by optic atrophy on the homolateral side. In another instance a radical antrum operation was performed, seemingly without anything unusual happening; however, se-

vere hemorrhage developed and the antrum was tightly packed; the vision in the homolateral eye was already completely lost when the packing was removed. In instances such as have been mentioned, several explanations come to mind. Cases of optic atrophy have been described following nasolacrimal sac surgery. In the ethmoidectomy case, the nerve may have been divided inadvertently. In the antrum case, arterial spasm may have been the responsible factor.

Orbital Injections and the Optic Nerve

Temporary loss of vision may follow the injection of procaine. When an anesthetic is injected into the orbit, the injection needle rarely enters the optic nerve. In a recent study, pronounced loss of vision followed the injection of 2 per cent procaine into the orbit; with 8 per cent procaine there was decrease in visual acuity within ten minutes, and a return in two hours. In 21 of the 40 cases in which a local anesthetic was injected into the orbit, there was some loss of vision: in 6, there was loss of light perception; in 6, loss was to shadow vision, and in 2 individuals the loss was limited to the nasal field (Carroll and de Roetth). In all cases reported to date, loss of vision from orbital injections of anesthetics was transient.

Alcohol has been injected into the orbit for relief of pain in many instances during the past few years. Usually the eye is sightless or has poor vision, and in these cases there is no worry regarding resultant loss of vision. Rarely, optic atrophy has followed the injection of alcohol.

Ocular Injuries from Air and Water Trauma

For some curious reason many persons fail to realize that air and water under pressure can inflict serious damage. I have notes on two cases. In one case, air under high pressure lacerated both eyelids and accounted for what amounted to an evisceration of one eye and loss of temporal field of the opposite eye. In the other case, a stream of water under high pressure accounted for loss of vision in both eyes, with atrophy of both nerves and very low final visual acuity in each eye.

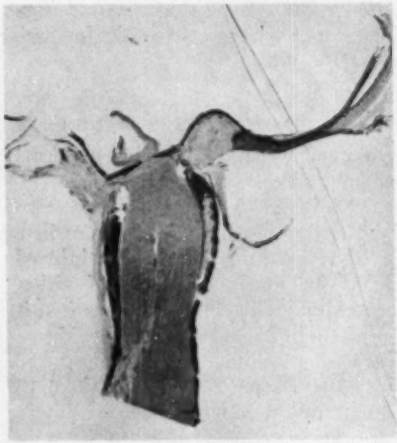

FIG. 3—Hemorrhages into optic nerve sheath. Subdural and subarachnoid hemorrhages can be differentiated here.

HEMORRHAGES INTO THE OPTIC NERVE SHEATHS

Hemorrhages develop within the optic nerve sheaths in many cases of subarachnoid hemorrhage, whatever the cause of the hemorrhage may be: ruptured aneurysm, vascular hypertension, or injury. Hemorrhage into the optic nerve sheaths may occur within the orbit when there has been no hemorrhage within the envelopes of the brain. It has been assumed that hemorrhage within the optic nerve sheaths may account for loss of vision. Some clinicians have used the term "subdural hematoma of the optic nerve sheaths" with the same connotation as subdural hematoma within

the cranial cavity. Extensive hemorrhages may be present within the optic nerve sheaths, although the vision may remain quite normal. Hemorrhages within the optic nerve sheaths may be associated with hemorrhages within the optic nerve substance. It seems established beyond reasonable doubt that blood from within the cranial cavity does not usually flow forward freely into the spaces about the orbital optic nerve. Some observers have assumed that since particles of India ink pass forward from the cranial cavity to the perioptic spaces, blood must also pass forward freely.

DECOMPRESSION OF THE OPTIC CANAL

In cases characterized by loss of vision associated with trauma, unroofing of the optic canal has its advocates. In this country we have had little or no experience with this procedure. It is difficult to assess any value it may have. The procedure in itself is traumatic, and certainly it cannot be indicated in many cases.

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XII

GENERALIZED NONINFECTIOUS DISEASES

JOHN WOODWORTH HENDERSON, M.D.

THE generalized noninfectious diseases of the optic nerve to be discussed will include those due to (1) blood dyscrasias, (2) blood loss, (3) allergy, (4) metabolic dysfunction, (5) inherited systemic disease, and (6) nutritional deficiency.

Blood Dyscrasias

Retrobulbar neuritis is found occasionally in the anemias, secondary as well as macrocytic. In pernicious anemia, cases have been reported with bilateral progressive visual loss, with associated central scotomas[2] or other field changes. Without treatment, optic atrophy may result. Refined liver extract or vitamin B_{12} are of equal value in treatment, but folic acid alone will not halt progressive neurological changes.[11] Adequate therapy maintains the blood at constantly normal levels, and 85 per cent of patients show improvement in their neurological manifestations on efficient treatment. Disc pallor may occur as the result of anemia alone and should be differentiated from atrophy.

The leukemias, anemias and polycythemias all produce swelling of the nerve head in certain cases (figs. 1, 2).[13] Although this response could be an accompaniment of venous dilatation from hypoxia or venous stasis, increased cerebrospinal fluid pressure is found often enough to suggest that the papill-edema may reflect the intracranial status.

Retrobulbar neuritis can also occur with leukemia. The importance of a complete blood count with differential smears must be emphasized in the complete survey of a patient with optic nerve disease.

Blood Loss

Loss of blood has been reported frequently as a cause of blindness. Two mechanisms exist. The first is sudden hypotension following acute hemorrhage; the other is secondary anemia after chronic blood loss. Visual symptoms usually follow gastrointestinal, renal, pulmonary or uterine hemorrhage. Repeated hemorrhages are more likely to cause difficulty than single episodes of massive bleeding.

Hypoxia appears to be the common factor affecting the optic nerve. If preexisting anemia and hypoproteinemia are aggravated by further bleeding, edema appears in the optic nerves. If the condition is unrelieved, optic atrophy results.

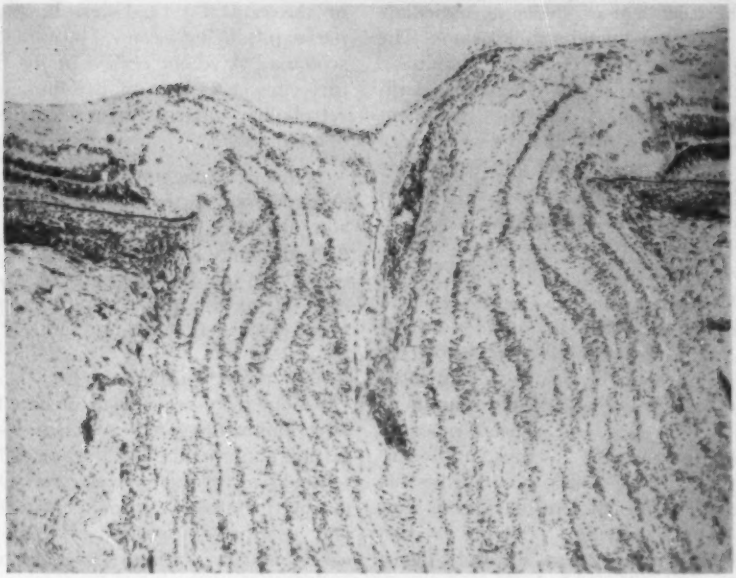

FIG. 1—Slight papilledema and leukemic infiltration of disc, resembling papillitis. (H & E; × 50) (Courtesy of Armed Forces Institute of Pathology.)

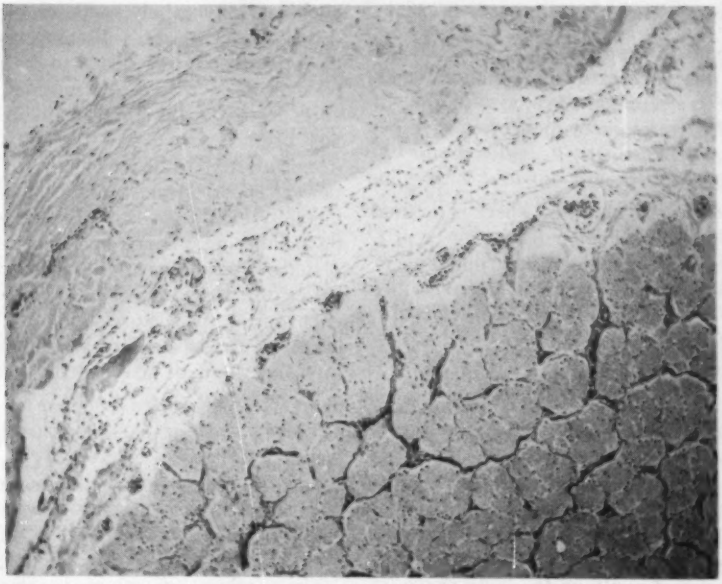

FIG. 2—Leukemic cells in pial vessels. (H & E; × 70) (Courtesy of Armed Forces Institute of Pathology.)

The treatment of choice is immediate and repeated blood transfusion. The prognosis is better in acute traumatic bleeding than in cases where visual involvement follows chronic recurrent hemorrhage by several days or weeks.[5] In most instances visual impairment after hemorrhage is observed in patients with previous ocular damage.[12]

Allergy

Allergic reactions have been shown to cause certain cases of optic neuritis.[4] Pork, turkey, chocolate and nuts have been implicated. Exposure to primroses and to poison ivy has elicited optic neuritis. Other cases have been reported after injections of tetanus antitoxin, antirabic vaccine and intracutaneous tuberculin.[14] One patient has been seen with optic neuritis following a bee sting.[8] In certain patients, the optic nerve may be affected as a part of a more generalized central nervous system reaction or as a manifestation of regional angioneurotic edema.

On theoretical grounds, it would appear that the treatment of choice for allergic retrobulbar neuritis might be ACTH, cortisone or meticorten therapy.

Metabolic Diseases

a. Diabetes mellitus. There is no final answer as to whether diabetes ever produces optic neuritis. When optic nerve involvement occurs, it may be from other causes, such as nutritional or vascular insufficiency, and all possible causes should be ruled out.

b. Thyroid disease. Retrobulbar neuritis has been reported as an accompaniment of hyperthyroidism. In the endocrine disturbance of thyrotropic exophthalmos or progressive exophthalmos, visual disturbance occurs infrequently. In such cases, increased orbital pressure acts either directly on the optic nerve or causes stasis in the region of entrance of the central retinal vessels into the nerve, producing a central or paracentral scotoma.[3] A recent review of the literature cites cases both of papillitis and of retrobulbar neuritis in endocrine exophthalmos.[1]

Medical management by thyroid administration, corticotropin or cortisone administration may suffice, but if blindness threatens, pituitary irradiation or orbital decompression may be considered. If no disc pallor results, the prognosis for visual return is better.[3]

Inherited Systemic Disease

Among the myriad systemic hereditary affections which produce ocular lesions, certain abnormalities of the skeletal system may affect the optic nerve.[10] Osteopetrosis (Albers - Schönberg disease) and osteitis deformans (Paget's disease), and its variants, leontasis ossea and hyperostosis frontalis interna, result in optic atrophy by narrowing of the optic canal. Craniofacial anomalies, such as oxycephaly and craniofacial dysostosis (Crouzon's disease) can lead to optic atrophy secondary to the papilledema of increased intracranial pressure. Recently, optic nerve involvement has been reported in Albright's syndrome (osteitis fibrosa cystica),[9] and a newer entity, Pyle's disease (cranial metaphyseal dysplasia), has been shown to include optic nerve involvement as a result of thickening of the membranous bones of the face.[6] The condition of pachyderma periostosis, in which the bones of the base of the skull are also involved, may be associated with foramenal closure.[7]

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XIII

NUTRITIONAL AMBLYOPIA

FRANK D. CARROLL, M.D.

NUTRITIONAL amblyopia was common during World War II among prisoners of war maintained on starvation diets by the Japanese. It was present also among American soldiers taken prisoner during the late Korean War.[4] It has probably occurred in all parts of the world where there has been serious malnutrition. The age at onset varies from infancy to old age. I have studied this disease in children in the British West Indies,[2] but I have never seen it among children in this country.

The American soldiers I examined had been taken as prisoners by the Japanese at Bataan or Corregidor.[2] They were given very little food of any kind, and within two or three months most of them had developed multiple deficiency diseases — often pellagra and beriberi. Their vision usually underwent gradual impairment. If in the early stages of this impairment the prisoner's diet improved, his vision sometimes improved. Usually, however, these men were left on inadequate diets for many months, and this resulted in permanent bilateral amblyopia with the following features: (1) reduction in visual acuity, frequently to 20/70 or less; (2) central or centrocecal scotomas; and (3) from slight to marked temporal pallor of the optic discs. A recent survey in Canada of 61 former prisoners of war with nutritional amblyopia indicates that there has been no significant change in their visual acuity between the time of their repatriation in 1946 and the time of the survey in 1955.[1] Autopsies on 11 former prisoners of war, who died of unrelated diseases, showed degeneration of the papillomacular bundle in four (figs. 1 and 2), and demyelination of the posterior columns of the spinal cord in seven (fig. 3).[3]

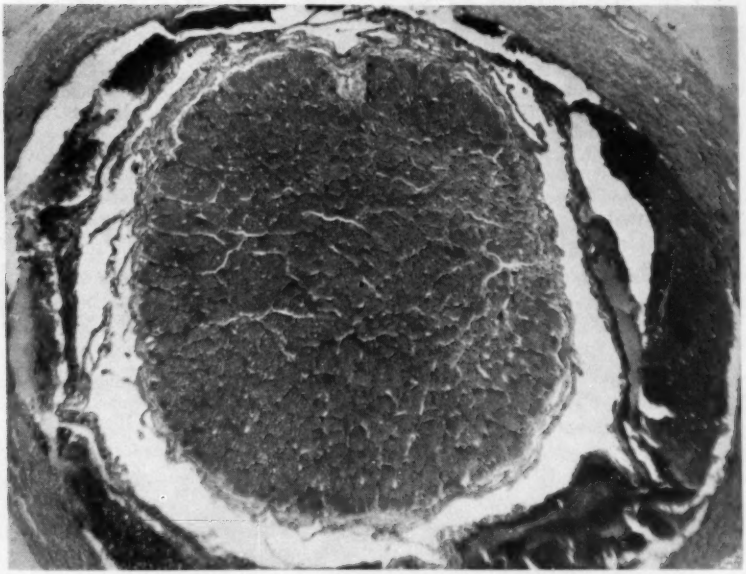

FIG. 1—AFIP Acc. 714830. Cross section of optic nerve showing a V-shaped area of atrophy on the temporal side. (Myelin stain; × 30) (Courtesy of Dr. Miller Fisher. His Case 1.)

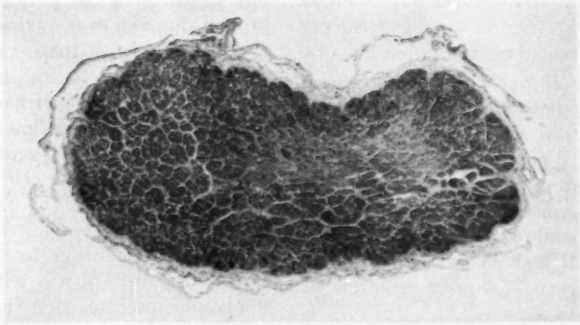

FIG. 2—AFIP Acc. 714830. Oblique section of optic nerve showing demyelination of axial bundles. (Myelin stain; × 22) (Courtesy of Dr. Miller Fisher. His Case 1.)

Other findings in nutritional amblyopia may include partial nerve deafness and widespread neurological involvement. Diarrhea or intercurrent infection may precipitate the onset of poor vision in an individual whose diet is inadequate. The etiologic factor is probably a lack of one or more of the components of the vitamin B complex. The best treatment seems to be a good diet sup-

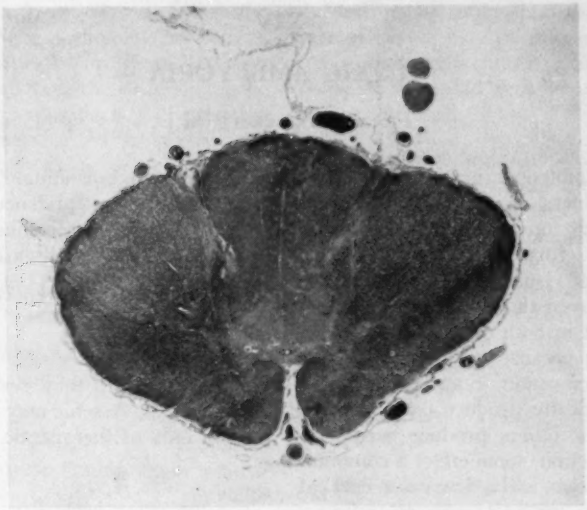

FIG. 3—AFIP Acc. 714830. Cross section of thoracic spinal cord showing demyelination of posterior columns. (Myelin stain; × 12.5) (Courtesy of Dr. Miller Fisher. His Case 1.)

plemented by large amounts of vitamin B complex. Brewer's yeast cured the disease in the children observed in the West Indies.[6]

Cases of nutritional amblyopia resulting from prolonged postoperative vomiting and from the pernicious vomiting of pregnancy have been reported.[5] A patient seen by me had received quinine for malaria and had then developed bilateral centrocecal scotomas. The quinine itself was, of course, not responsible for this development. Questioning revealed that the patient had lost over twenty pounds during his acute attack of malaria. A good diet and vitamin B complex soon restored normal vision and full visual fields. It is not unlikely that "alcohol amblyopia," which is to be discussed in the section on toxic amblyopia, is identical with nutritional amblyopia.

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XIV

TOXIC AMBLYOPIA

FRANK D. CARROLL, M.D.

TOXIC amblyopia is partial or complete blindness caused by some toxic agent which interferes with the function of the retina, the optic nerve, or the more central visual pathway. In cortical blindness, even though the vision is totally absent in both eyes, the pupils react to light because the lesion is above the pupillary center. Some toxic agents characteristically produce central visual field defects, others produce peripheral field contraction, some effect a combination of the two, and a few cause cortical blindness.

In the history of a patient with optic nerve disease, any known exposure to poisonous chemicals at work or at home should always be included. These substances may be inhaled, ingested, or absorbed through the skin. For reference purposes, the noxious agents discussed in this outline will be listed in alphabetical order (table I) with references to original articles concerning them.

Aniline dyes may be absorbed through the skin, as from freshly stamped diapers in a hospital nursery,[60] or they may be inhaled, as in the fumes and fine dust of aminobenzol. In either event, methemoglobinemia with marked cyanosis may result, with both peripheral contraction of the visual fields and central scotomas.[40]

Anoxia causes cortical blindness, which may be temporary or permanent depending on the duration and severity of the anoxia. The anoxia may occur during anesthesia, with or without cardiac arrest,[57] in association with apnea during an asthmatic attack,[51] or in carbon monoxide poisoning.[49] Anoxia may also produce the optic neuritis seen in carbon monoxide poisoning and, occasionally, in vascular disease.

Antabuse has been reported as a cause of retrobulbar neuritis.[66]

Arsenic in either the trivalent or pentavalent form may result in severe optic neuritis. Arsenic may be a constituent not only of therapeutic drugs but of dyes, cosmetics, and insect sprays and food contaminated by them. Complications include dermatitis, conjunctivitis, gastroenteritis, nephritis, and polyneuritis.[35] When such subjective symptoms

TABLE I

50 CAUSES OF TOXIC AMBLYOPIA

Analine	Marihuana
Anoxia	Mescaline
Antabuse	Methyl alcohol
Arsenic	Methyl bromide
Aspidium	Mushroom poisoning
Atabrine	Optochin
Barbital	Paraminosalicylic acid
Benzene	Plasmocide
Bromides	Prestone
Carbon disulfide	Quinine
Carbon monoxide	Salicylates
Carbon tetrachloride	Santonin
Chloromycetin	Sodium iodoacetate
Digitalis	Snake bite
Dilantin	Spinal anesthesia
Dinitrobenzene	Stramonium
Diphtheria Toxoid	Streptomycin
Ergot	Sulphonamides
Ethyl alcohol	Tansy
Ethyl pyridine	Thallium
Finger cherries	Tobacco
Hair dye (coal tar)	Toluene
Hexamethonium	Trichlorethylene
Iodine	Tridione
Lead	Tryparsamide

as blurring, "heat waves from the street," and light flashes are noticed, as sometimes occurs before there has been any visual field loss, the drug should be stopped. Tryparsamide is still used for sleeping sickness in Africa and is still being reported as a cause of optic atrophy.

The normal concentration of arsenic in the body is as follows:

Blood: 0.03 to 0.06 mg. per 100 cc.

Urine: 0.03 to 0.065 mg. per 24 hours.

BAL (British Antilewisite) is valuable in the treatment of arsenic poisoning.[29,31]

Aspidium (the male fern), an anthelmintic, may cause temporary or permanent blindness. Contraction of the fields may be a final result. Inexplicable is the frequency with which unilateral cases of this type of amblyopia occur.[2,10,43]

Atabrine, which is used for both the prevention and the treatment of malaria, has apparently occasionally induced scotomas[27] and has involved the cornea as well.[1,78]

Barbital may infrequently cause either a centrocecal scotoma or peripheral field contraction or even central blindness.[52]

Benzene[58] and its derivatives, which may be components of paints, insecticides, solvents, and explosives, are known to have caused aplastic anemia, encephalitis, optic neuritis, and optic atrophy. Specifically, benzene hexachloride,[28] nitrocellulose paint,[89] dinitrobenzene,[75] and TNT have produced optic neuritis. Retinal hemorrhages may be induced by these substances.

Bromides[82] may result in such visual hallucinations as the seeing of trees, flowers, men, and animals.

Carbon disulfide, which is used in many industrial processes, including the vulcanizing of rubber and the manufacture of rayon, may produce central scotomas and contraction of the peripheral fields. Widespread neurological involvement may result.[41,63]

Carbon monoxide poisoning causes anoxia (see above), and the anoxia in turn may cause blindness. Optic atrophy has been reported, but much more frequently the cortex is involved and the pupils react to light in spite of complete absence of vision. The two cases I have observed personally recovered entirely,[93] but other reported cases have developed homonymous hemianopsia,[54] marked reduction in visual acuity,[49] or rarely, optic atrophy.

Carbon tetrachloride may be inhaled or taken by mouth as an anthelmintic, and is known to have induced constriction of the fields and optic atrophy.[39,53,61,92]

Chloromycetin (chloramphenicol) administered over a period of months has caused at least three cases of optic neuritis. In one patient[73] vision in both eyes became nil, but ultimately vision in the right eye was restored to fingers at 2 feet, and vision in the left eye to 20/200. In the other two patients,[62,102] vision eventually returned to normal, but in one case only after a year's time.[62] In a single series recently reported,[83] aplastic anemia developed in 33 patients treated with chloromycetin.

Digitalis frequently causes visual hallucinations.[15] Patients say that "everything looks bright and glary," or that objects seem to "have snow on them"; occasionally green, blue, or yellow vision is described; "flashes of light," "stars," "gold fish" are other complaints. These visual symptoms may occur even when patients are on what is usually considered the "normal" dosage of digitalis or its derivatives, and they may be the only manifestation of intoxication.

All complaints disappear when the drug dosage is decreased. Retrobulbar neuritis with central scotoma has been known to occur.[56,98]

Dilantin may cause central scotomas with reduction of visual acuity, with recovery when the drug is stopped.[76]

Dinitrobenzene.[75] See *Benzene.*

Diphtheria toxoid may produce optic neuritis in a hypersensitive individual.[87,91] Horse serum, tetanus toxoid, chocolate, pork, fish, and turkey are other agents which are known to have induced allergic optic neuritis.

Ergot has been reported as a cause of contraction of the visual fields and central scotomas, associated with constriction of the retinal vessels and edema.[46]

Ethyl alcohol taken by mouth may in rare instances induce an acute alcoholic amaurosis,[19] a central type of total blindness from which recovery usually occurs within twenty-four hours. When injected intravenously, ethyl alcohol has apparently caused permanent bilateral central scotomas.[80] Much more commonly, of course, this agent is associated with a chronic form of toxic amblyopia which has been known as "tobacco-alcohol amblyopia," but which may occur in patients who never have used tobacco in any form.[18] This "alcohol amblyopia" is characterized by bilateral centrocecal scotomas and should probably be considered a nutritional amblyopia.[14,16,17] Recovery is often complete if the patient takes large doses of vitamin B complex even though he continues his usual intake of alcohol.

Ethyl pyridine, an intermediary product in the manufacture of isonicotinic acid hydrazide, is said to have induced amblyopia.[84]

Finger cherries (Australia) have caused sudden blindness.[50]

Hair dye ("Glo-Ruz") is a coal tar dye, and its use is known to have been followed by papillitis and reduced vision.[69] Central scotomas from other hair dyes have been reported.[7]

Hexamethonium, used in the treatment of hypertension, has resulted in retrobulbar neuritis within a few minutes of its injection intramuscularly.[13] The bilateral blindness induced has been permanent. Unilateral blindness was reported in a patient who received hexamethonium iodide while receiving a general anesthetic administered with a facial mask.[59] This may have been due to a closure of the central retinal artery associated with pressure on the eye during administration of the anesthetic, plus the low blood pressure produced by the drug.

Iodine, administered intravenously as Pregle's solution, has induced blindness. Vision returned but there was contraction of the field, central scotoma, and retinopathy.[26,37,38]

Lead poisoning may cause papilledema, optic neuritis, retinopathy, or even central blindness. Children who have eaten lead paint off their cribs have developed lead encephalopathy and optic atrophy. Lead in nipple shields, face powder, and dried-out paint has also caused optic atrophy in children. Adults have been poisoned from the burning, as fuel, of old wooden automobile batteries, and from the use of lead paint, tetraethyl gasoline, lead pipe,[103] cosmetics, food cooked in lead containers, insecticides (especially lead arsenate[34]) and even from the use of electric teapots.

The normal concentration of lead in the body is as follows:

Blood: 0.02 to 0.08 mg. per 100 gm.
Urine: 0.02 to 0.08 mg. per 24 hours.

The best treatment for lead poisoning is probably the administration of the chelating agent, calcium disodium versenate

(ethylene diamine tetra-acetic acid).[25] A test dose of 250 mg. is given by mouth; if no allergies or other symptoms develop within twenty-four hours, 2 grams a day are given in divided doses for seven days.

Marihuana may create purple vision and striking visual hallucinations.[45]

Mescaline (peyote), used as a "truth drug" in World War II, can cause visual hallucinations somewhat resembling those arising from the use of digitalis. Flashes of light, flickering, and increased vividness of colors have been mentioned.[99]

Methyl alcohol usually induces amblyopia in eighteen to forty-eight hours after ingestion, but blindness has also resulted from the following: (1) Inhalation of fumes, as from an alcohol lamp, and in another instance from large beer vats that were treated on the inside with a varnish containing wood alcohol. There was little ventilation and the painters were poisoned. (2) Absorption through the skin: (a) the alcohol with which an infant was sponged daily was discovered to be methyl alcohol when the baby became blind; and (b) an engineer using a solution daily to clean his hands became totally blind; the solution was found to be wood alcohol and the blindness completely disappeared in twenty-four hours.

Any patient who has a sudden onset of poor vision, abdominal pain, nausea, and vomiting should be considered as a possible victim of methyl alcohol poison. If the pupils are dilated and fixed, the prognosis for life is poor.[6] The fundus picture may be normal, or there may be a papillitis with peripapillary edema. Often optic atrophy develops, sometimes with deep cupping. Although there is some difference of opinion as to whether acidosis is related in any way to the loss of vision,[55,86] all authorities seem to agree that the present treatment of choice in serious cases is the intravenous and oral administration of alkalies. The carbon dioxide combining power of the blood is a valuable indication of the course and prognosis. In one series of cases, all patients with less than 10 milliequivalents per liter died.[6] All with normal blood carbon dioxide (above 26 milliequivalents per liter) recovered. If sterile bicarbonate solutions are not available, ordinary bicarbonate of soda from freshly opened boxes may be added to flasks of sterile water, saline, or glucose solution to make a solution of 25 to 50 gm. of bicarbonate per liter. Alkali therapy should be continued for at least three days, with frequent check of the blood carbon dioxide or of the urine. Large, dense, bilateral centrocecal scotomas are most common, but arcuate, central, or paracentral defects are also found. The visual field may be entirely lost in the early stages and may never be recovered, or it may be recovered, and then, over a period of months, may decrease in size again.

Methyl bromide,[23,48,88] which is used in fire extinguishers, *methyl chloride*,[79] which is used in refrigerators, and *methyl iodide* have all caused partial or complete optic atrophy. *Methyl mercury* compounds have caused constriction of visual fields and deafness.[67]

Mushroom poisoning has resulted in temporary blindness associated with transient vascular hypertension.[20]

Optochin, a derivative of quinine, was formerly used extensively and caused central scotomas with or without peripheral contraction.[70,96]

Paraminosalicylic acid (PAS) is reported to have caused a drop in vision during a course of treatment for pulmonary tuberculosis.[95]

Plasmocide, used in the prevention and treatment of malaria, has induced amblyopia.[8,30]

Prestone (ethylene glycol), an "antifreeze" used in automobile radiators, has caused blindness and sometimes death when taken by mouth.[85] Five soldiers who drank this solution became almost totally blind.[12]

Quinine has frequently produced total loss of vision, followed by partial or complete return of vision but with the fields often permanently constricted. Even a dose as small as one grain is said to have produced transient blurring in sensitive individuals.[42] The fundi may appear normal in the earliest stage, but edema of the retina[21] and narrowing of the retinal vessels supervene. Therapeutic blocking of the stellate ganglion and vasodilators have been applied but their value is questionable.[4]

Salicylates in large doses may cause symptoms similar to those attributable to quinine,[90] but the prognosis is usually better.

Santonin may induce zanthopsia or violet vision.[44]

Sodium iodoacetate causes degeneration of retinal rods and, later, of the cones in animals, and *sodium iodate* produces degeneration of the pigment epithelium and choroidal inflammation.[81] The intravenous injection of "septofod" (a German preparation for puerperal sepsis which contains sodium iodide and free iodine) has caused blindness.[94]

Snake bite has been followed by loss of sight.[32]

Spinal anesthesia has in my experience caused two cases of retrobulbar neuritis and sixth nerve paralysis, Recovery was complete.[5]

Stramonium, used in cigarettes for asthma, has resulted in bilateral centrocecal scotomas.[47] In the form of "jimson weed," it is brewed, especially by natives of the West Indies, into a concoction used for asthma and colds. In my experience this "tea" has caused coma and widely dilated pupils, due to its atropine-like effect. Injections of pilocarpine may be helpful, but death has occurred.[65]

Streptomycin, a common cause of deafness, has also been known to damage the optic nerve. The induced retrobulbar neuritis, with small central scotomas, has completely disappeared on discontinuance of treatment.[97] In attempting to evaluate the numerous other cases that have been reported,[3,11,68,74,77,91,105] I have sometimes found it difficult to decide whether the optic nerve involvement was due to tuberculosis or to the drug used to treat it. Zanthopsia may occur.[104]

Sulphonamides may cause optic atrophy and retinal hemorrhages. Temporary central scotomas have been recorded.[22,106]

Tansy (in tansy tea) has caused delirium and on recovering from this the patient has had a homonymous paracentral scotoma.[64]

Thallium is a very toxic agent which causes peripheral neuritis, optic atrophy, encephalitis and loss of hair. One patient developed this syndrome after taking thallium sulfate by mistake instead of table salt. The poison was being used for the control of cockroaches and rats and had the same appearance as ordinary sodium chloride. The husband and child of this patient had temporary loss of hair. Thallium formerly was used as a depilatory and caused many cases of optic atrophy. Even now numerous poisonings are reported.[9,36,72]

Tobacco amblyopia, characterized by bilateral centrocecal scotomas which come on gradually, may occur in nondrinkers.[14,18] If the patient discontinues smoking, his vision usually improves. But if he continues to smoke and takes large doses of vitamin B complex and a well-balanced diet, there will usually be improvement over a period of months in

spite of the smoking. Diabetics are somewhat more apt to develop tobacco amblyopia than nondiabetics, probably because some of them are on diets, the essential food elements of which are on the borderline of inadequacy.

Toluene may produce the same condition as that produced by benzene.

Trichlorethylene, which is occasionally used as an anesthetic and in industry as a solvent and cleaning agent like carbon tetrachloride, may cause anesthesia of the fifth nerve, optic neuritis, peripheral neuritis, and central nervous system involvement.[36,71]

Tridione appears to interfere with the light adaptation of the retinal cones.[33] Patients complain of a dazzling whiteness, as though objects were covered by snow, as in digitalis intoxication. In the shade, objects appear normal. Visual acuity may be 20/20 on an unlighted test chart but 20/100 when the chart is illuminated.[100]

Tryparsamide. See *Arsenic.*

This list of 50 etiologic agents which produce toxic amblyopia is not complete but is believed to include the more important causes. As new drugs are used in medicine, and new industrial processes are developed, we must be constantly on the alert for new causes of toxic amblyopia. In this country, for example, tryparsamide is becoming an item of historical interest only, but meanwhile such new drugs as chloromycetin, streptomycin, and hexamethonium are constantly being added to the list.

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XV

TUMORS OF THE OPTIC NERVES AND CHIASM: DIFFERENTIAL DIAGNOSIS

FRANK B. WALSH, M.D.

PRIMARY tumors of the optic nerve and its sheaths are uncommon. In a large series, optic nerve tumors and malignant choroidal tumors had a ratio of 1:200 (Verhoeff). Intrinsic optic nerve tumors are also rare when compared with tumors which involve the optic nerves and chiasm through pressure or through interference with circulation. In occasional instances tumors of the optic nerve may be visible on ophthalmoscopic examination, but usually the diagnosis is made on the basis of several examination findings. Intrinsic optic nerve tumors are considered under two headings: (1) tumors involving the optic disc; (2) tumors involving the stem of the nerve and optic nerve sheaths.

TUMORS INVOLVING THE OPTIC DISCS

Melanomas

Pigmented areas immediately adjacent to the optic disc, or on or within it, often have no particular significance and represent an abnormality of develop-

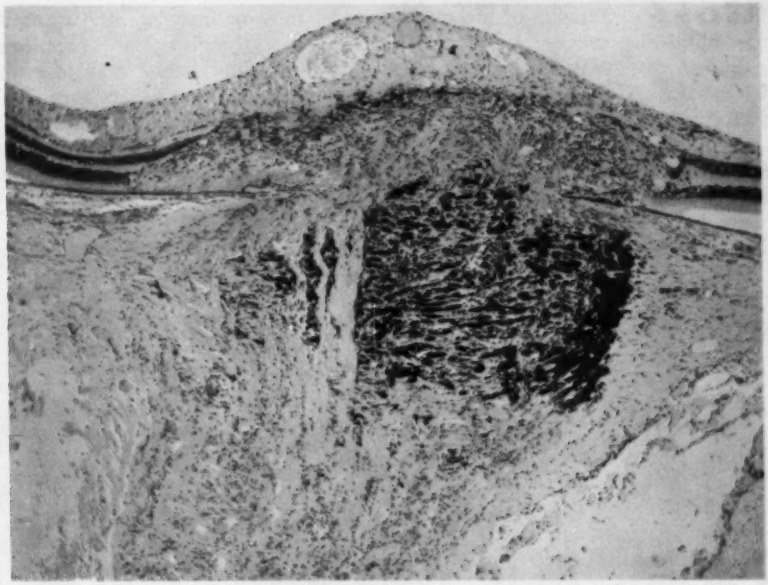

FIG. 1—Congenital pigmentation of the optic nerve in 13-year-old white girl. (AFIP 26439, Acc. 683407) (Courtesy of Dr. Michael J. Hogan.)

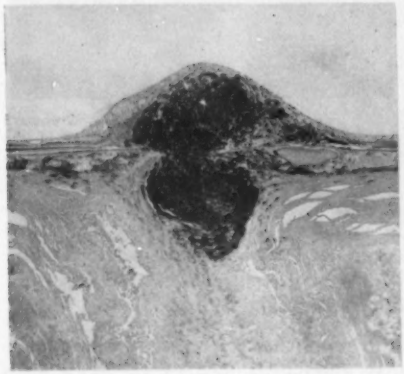

FIG. 2—Melanoma of the optic disc in a 33-year-old Negro woman. (AFIP Acc. 683403) (Courtesy of Dr. Michael J. Hogan.)

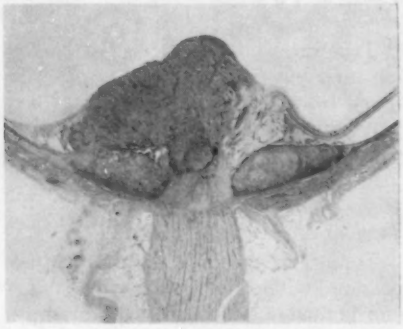

FIG. 3—Juxtapapillary choroidal melanoma invading the optic disc. (AFIP Acc. 514792) (Courtesy of Dr. Robert P. Dennis, Lawton, Okla.)

ment. The lamina cribrosa contains scleral and choroidal elements, and in consequence pigmented cells may be present in it. Congenital melanosis may be associated with pigment change in the optic disc (fig. 1). Melanomas involving the optic disc occur most frequently in Negroes (fig. 2). This is of particular interest, since malignant melanomas of the choroid occur relatively rarely in Negroes.

There are few examples of melanoma of the optic disc; such reported cases usually represent tumor of the choroid which has invaded the optic disc (Cordes and Hogan) (fig. 3). In cases in which the melanoma has originated within the optic disc, there have not been metastases. The problem regarding malignancy in these tumors is very similar to that which surrounds infiltrating adenoma of the pituitary, in which there is local infiltration and anaplasia but absence of metastases (Jefferson).

Gliomas, Meningiomas

Gliomas and meningiomas may involve and seemingly originate from the optic disc. There is nothing which differentiates them on ophthalmoscopic examination (figs. 4 and 5). Gliomas are seen more often than meningiomas. Neurofibromas affecting the optic disc have been described; probably such tumors actually fall into the glioma or meningioma category.

Vascular Tumors Involving the Optic Discs

True angiomas of the optic disc occur infrequently. They must be differentiated from newly formed vessels which may have originated as a result of glaucoma (fig. 6).

Differential Diagnosis: Tumors of the Optic Discs

Tumors of the optic disc vary in appearance within wide limits (fig. 7). Tumor limited to the optic disc occurs rarely. Often in what may be termed pseudotumor of the disc there is a history of defective vision in the affected eye during the lifetime of the patient, and the appearance of the disc has remained unchanged. The following involvements of the disc may be confused with tumor:

1. Hyaline bodies in the optic discs, which always occur anterior to the lamina cribrosa, may be difficult to diagnose. In some instances, the appearance of the disc strongly suggests papilledema, and the hyaline bodies may be entirely covered when the abnormality is first noted. Ultimately such bodies become visible. Hyaline bodies in the optic discs or in the retina may be a manifestation of tuberous sclerosis. They may also occur as a familial anomaly. Hyaline bodies may be present in the disc and elsewhere in the retina.

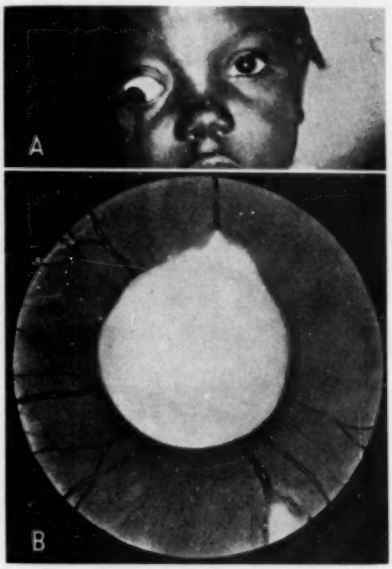

FIG. 4—(A) Patient with exophthalmos downward and laterally. (B) Drawing of the tumor of the disc. (Wilson and Farmer)

2. Persistent Bergmeister's papilla may simulate tumor of the optic disc (fig. 8). In such cases there may be pigmentation of the disc.

3. Medullated nerve fibers may occasionally suggest a mass in the disc.

4. Masses of fibrous tissue on the disc, with or without cystic formation, may represent an abnormality of devel-

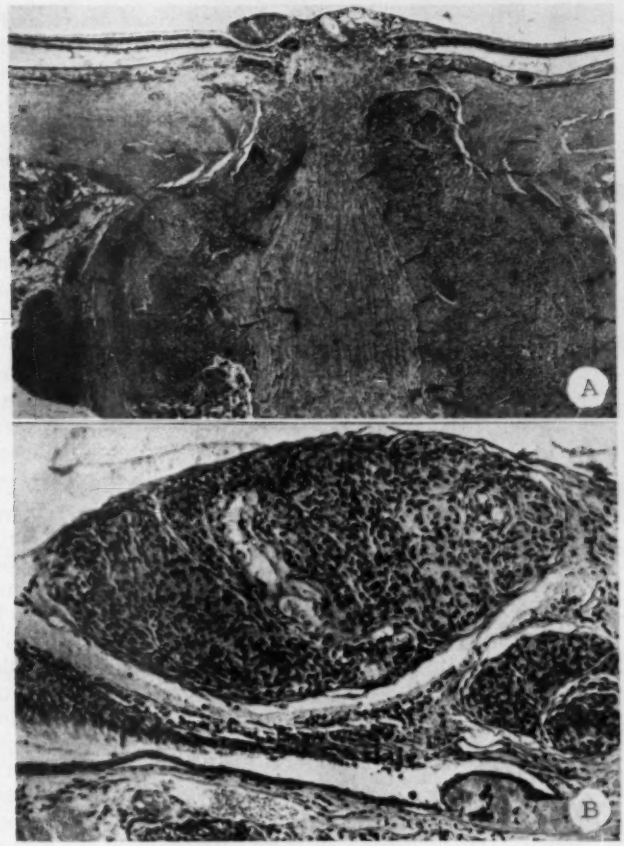

FIG. 5—Meningioma of the optic nerve. (A) Cross-section of the optic nerve and disc, showing invasion by the tumor. (B) High power magnification of the tumor cells on the temporal edge of the disc. (Coston)

opment (figs. 9 and 10). In some such instances it is impossible to differentiate from tumor with the ophthalmoscope.

TUMORS INVOLVING THE OPTIC NERVES AND OPTIC NERVE SHEATHS

Gliomas of the Optic Nerve

Gliomas of the optic nerve and chiasm may be associated with neurofibromatosis, a fact which has been known for many years, but which has relatively recently been stressed by Davis and by Marshall. When loss of vision occurs in an individual exhibiting neurofibromatosis and café au lait patches or in whom there is a familial trait of von Recklinghausen's disease, the possibility of glioma of the nerve or chiasm should come to mind at once. This curious association is present in a minority of cases of glioma of the optic nerve and chiasm (about 16 per cent according to Marshall; almost exactly the percentage in my experience). A majority of such tumors are

astrocytomas, but all types of glial tumor may be encountered — hence the value of the noncommittal term, gliomas (fig. 11).

FIG. 6—Vascular tumor involving the optic disc. Drawing of nerve head and surrounding retina, showing migration of pigment cells along walls of vessels. (Wyburn-Mason)

Site of Origin. A small minority of gliomas originate in the optic disc. In a majority of instances, gliomas of the optic nerve originate in the orbital portion of the nerve, possibly because this is the longest segment of nerve. In our experience, the tumor involves the chiasm about as often as it does the nerve. Obviously the site of origin, whether nerve or chiasm, in many instances is uncertain.

Age at Occurrence. Usually glioma of the optic nerve or chiasm makes its appearance known during the first decade of a child's life. Certainly 80 to 90 per cent develop within the first two decades.

Loss of Vision. This is an early symptom. When the glioma is within the orbital nerve, loss of vision may be present for months or years and for long periods before proptosis develops. Loss of vision in these cases is likely to be overlooked. The child usually does not exhibit any evidence of visual defect, and not infrequently the trouble is brought to light during routine examinations prior to school attendance.

Visible Atrophy of the Optic Disc. This is commonly present. Edema of the optic nerve head may be a pronounced feature. This may indicate involvement of the orbital nerve close to the globe. Pallor of the optic disc is seen more often than disc edema, since the tumor is usually situated in the posterior orbit or chiasm.

Proptosis. This is a characteristic feature when the tumor is within the orbit. The protrusion of the eye tends to be forward, or forward and downward.

Enlargement of the Optic Canal. This is a most important roentgenographic finding, indicating in many instances that there has been spread of tumor from the orbit into the cranial cavity. A diameter of 7 mm. seems to be the upper limit of normal; actually, a pronounced difference between the size of the two canals is most important in diagnosis (Pfeiffer). It is important to know that extension of an intrinsic tumor from the orbit into the cranial cavity may occur in the absence of pronounced enlargement of the optic canal, as we have observed in a proved case of meningioma.

Extension of Tumor. This may be recognized from a study of changes in the visual fields. With loss of vision in one eye and loss of the temporal field in the opposite eye, it is obvious that the tumor has extended backward to involve the chiasm. With a bitemporal defect and a subsequent loss of vision in one eye, it is clear that the tumor involving the chiasm has spread forward to one optic nerve.

Meningiomas (Endotheliomas, Arachnoid Fibroblastomas)

Meningiomas originate in the arachnoid sheaths. Such tumors involving the

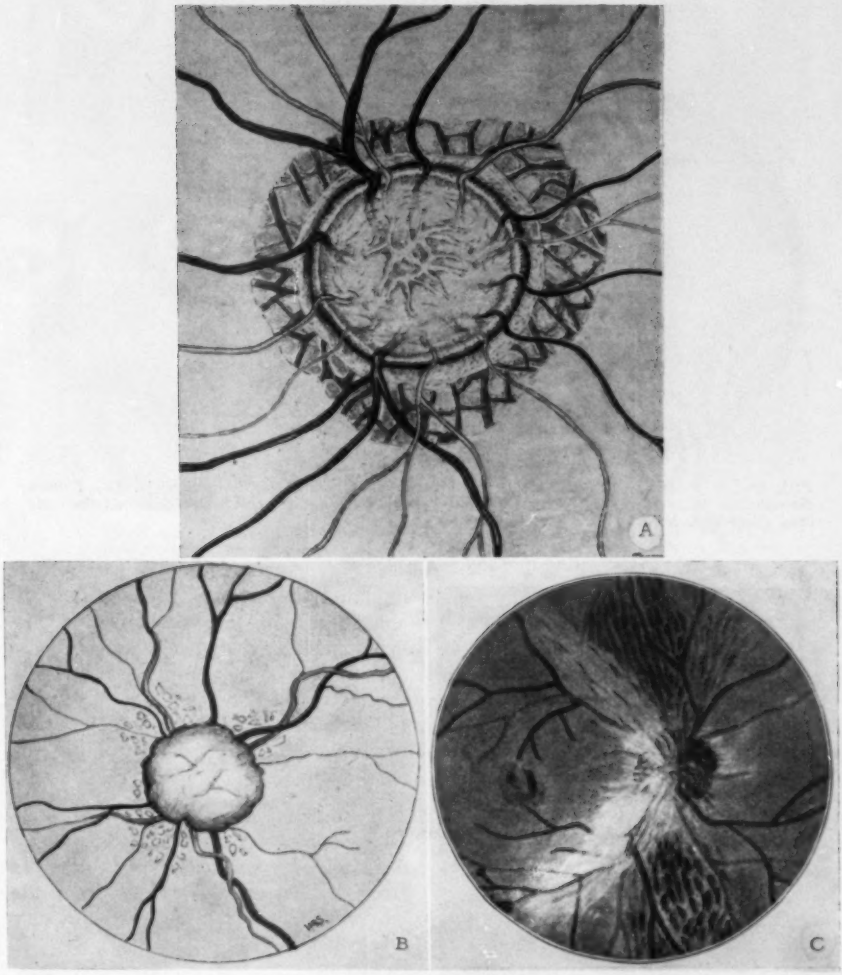

FIG. 7—Disc involvement in neurofibromatosis. Appearance of the optic disc (A) in patient of Trueman and Rubin; (B) in patient of Stllard; (C) in patient of Goldsmith.

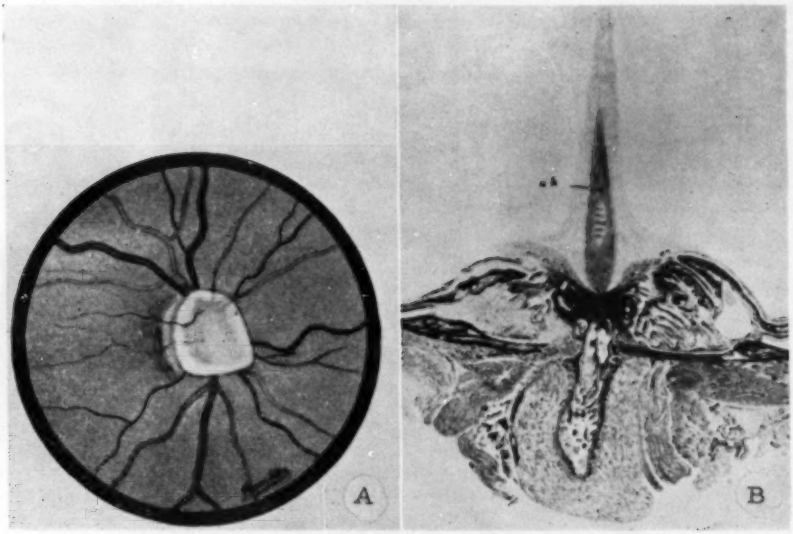

FIG. 8—(A) Persistence of Bergmeister's papilla in man, without persistent hyaloid. (B) Section through disc of an adult with persistent hyaloid artery (ah) and aberrant retina tissue on the optic disc. (Seefelder, Mann)

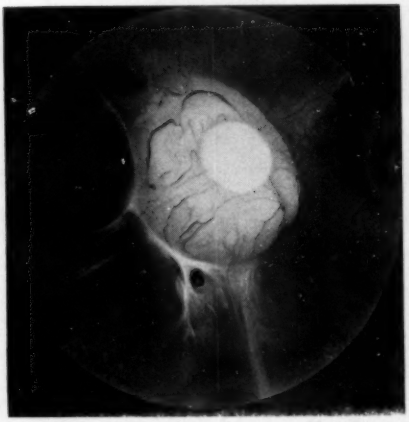

FIG. 9—A cystic-appearing mass involving the optic disc. The eye was blind from birth or early childhood. (Courtesy of Dr. E. Burton.)

optic nerve may originate in the orbit but rarely are entirely confined to the orbit. However, sections are available in the Armed Forces Institute of Pathology, and at least one specimen is available at the Johns Hopkins Hospital. The symptomatology of meningiomas of the optic nerve and chiasm is essentially similar to that of the gliomas, already described. Probably vision is lost earlier because of gliomas than because of meningiomas.

Most meningiomas which are of interest to ophthalmologists do not arise from the optic nerve sheaths but originate from the sphenoidal ridge, from the tuberculum sella, or in the olfactory grooves.

Fibromas

Fibromas are rare. They closely resemble, or actually represent, pseudotumors.

Metastatic Tumors

Metastatic tumors which involve the choroid and retina may involve the optic nerves. Loss of vision is a prime symp-

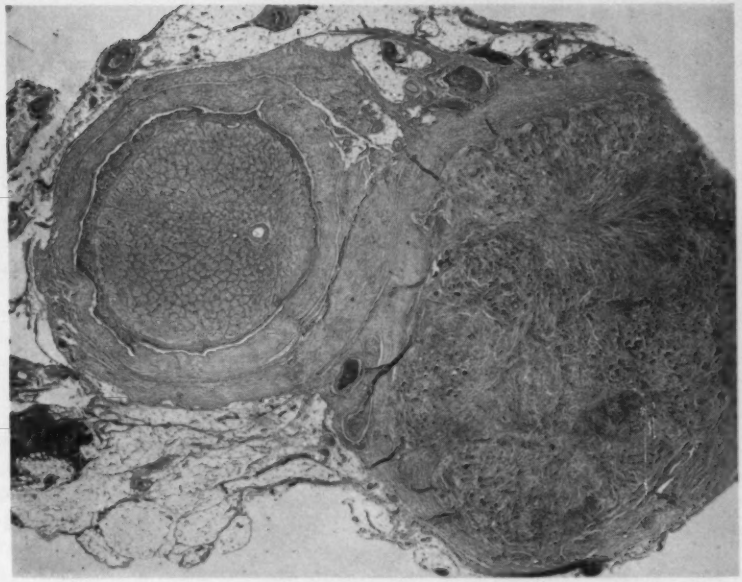

FIG. 10—Congenital anomaly with overgrowth of glial tissue in orbital cyst. The patient was a mentally defective white male, age 1 year. (AFIP Acc. 497440) (Courtesy of Dr. A. B. Crites, Kansas City, Mo.)

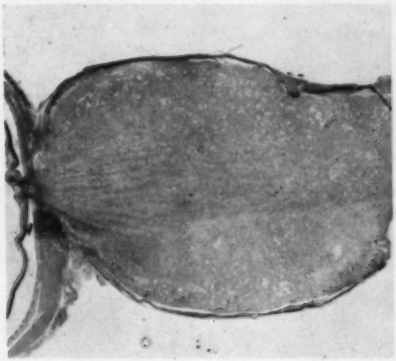

FIG. 11—Glioma of optic nerve. (AFIP 269268—55-17314)

tom when the nerve is involved, but metastasis to nerve sheaths may not produce loss of vision. Metastatic tumors develop within the optic nerve after transportation of tumor cells via the blood stream. Carcinoma of the breast is the type of tumor most frequently metastasizing to the optic nerve in women; and bronchogenic carcinoma, in men.

Retinoblastomas

These tumors, when they have extended centralward, infiltrate the nerve for only a few millimeters beyond the lamina cribrosa to the level of the central vessels; then further extension is into the subarachnoid space with further posterior spread, finally amounting to a tumor meningitis (fig. 12).

ROENTGENOGRAPHY AND OPTIC NERVE TUMORS

The size of the orbit may be increased on the side of the tumor. Changes in density of the soft tissue as a result of increased intraorbital pressure are likely

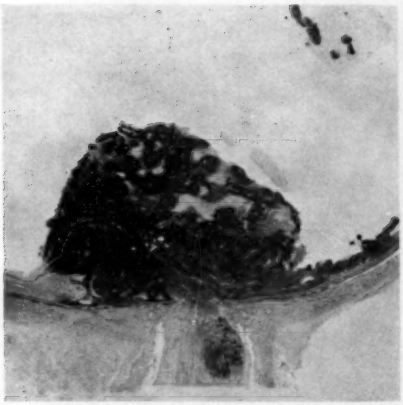

FIG. 12—Retinoblastoma. Spread is via nerve to level of entrance of central retinal vessels, then around optic nerve, and finally accounting for tumor meningitis. (AFIP Acc. 85270—55-18048)

to be difficult to evaluate. There may be indentation of bone; dehiscences in the bone; erosion of bone; hyperostosis; deformation and enlargement of the optic canal (Pfeiffer). Enlargement of the optic canal is important roentgenographic evidence of tumor when associated with loss of vision. With chiasmal glioma, both canals may be widened. Oftentimes there is doubt regarding the etiology of unilateral blindness which has occurred during childhood. If in such a case the blindness has been due to birth injury, the optic canal may be small. If tumor is the cause of blindness, the canal will probably be large.

DIFFERENTIAL DIAGNOSIS: OPTIC NERVE TUMOR

Attention has already been given to the differential diagnosis of ophthalmoscopically visible tumors of the optic disc. Abnormal developmental states must be recognized as such: medullated nerve fibers; prepapillary and epipapillary membranes; persistent Bergmeister's papilla; gliosis and cyst formation at the disc; colobomas; hyaline bodies. Choroiditis juxtapapillaris may be confused with tumor of the disc. It is to be recalled that tumor of the optic nerve may account for optic atrophy and pallor of the optic disc, or that it may account for disc edema.

Differentiation between tumor of the optic nerve and chiasm and optic neuritis may be difficult, and in some instances, for a time, impossible. What follows is written on a basis of personal experience, and in consequence, all possibilities are not mentioned.

Sudden loss of vision in one or in both eyes, with or without pain on movement of the eyes at the outset, and with central field defect, leads, usually correctly, to a diagnosis of optic neuritis not associated with tumor. However, sudden loss of vision may occur in one or in both eyes with intracranial tumors. Hemorrhage into a pituitary adenoma has been known to do just this. In some such cases there is no hemorrhage in the pituitary adenoma but rather a sudden swelling which has occurred for reasons unknown. In such cases of sudden loss of vision, with pituitary tumor there is likely to be an equally sudden development of external ophthalmoplegia. As a result of operation, recovery of vision with disappearance of the ophthalmoplegia has occurred in two cases with which I am familiar. Sudden loss of vision has occurred in children who have harbored a craniopharyngioma. Obviously in such instances there may have been loss of vision for a longer period than had been realized. Sudden loss of vision has been associated with ectopic pinealoma (Horrax and Wyatt; Baker and Rucker). Ordinarily we anticipate some recovery of vision with optic neuritis, not with tumor. Persistent loss of vision occurs as a result of optic neuritis in some instances, and in other cases as a result of tumor. In occasional cases of optic neuritis, recovery of vision may

occur as long as two or three years after the onset of the loss, according to Carroll's and my observations.

Recovery of vision after sudden loss would seem to justify a diagnosis of optic neuritis. It would not be anticipated with tumor affecting the optic nerves or chiasm. Spontaneous recovery of vision with intrinsic optic nerve tumors probably never occurs. With tumors affecting the optic nerve or chiasm, some degree of recovery from loss of vision may suggest a false diagnosis of optic neuritis. We have observed loss of vision and development of a central field defect in a woman during her first pregnancy. After delivery the vision returned to normal and the scotoma disappeared. During a subsequent pregnancy she again lost vision and exhibited a central field defect. Later she developed localizing bitemporal field defects, and at operation a suprasellar meningioma was removed. It is generally well known that pregnancy may activate meningiomas. In the case of a young child, there had been sudden loss of vision, and the child seemed quite blind when first seen. There was no history of any recent illness. It seemed reasonable to wait for developments. In two weeks time it was reported that the visual acuity had returned so that the child could pick up very small objects from the floor. We congratulated ourselves on the conservative handling of the problem. A year later there was tremendous hydrocephalus and pronounced optic atrophy with total blindness. At operation, a large craniopharyngioma was encountered.

As regards scotomas, much could be said concerning differential diagnosis, but only a few points are made here. Central scotomas characterize many, but by no means all, cases of optic neuritis (Chamlin). Central scotomas occur with some tumors which involve the chiasm and optic nerves. With pituitary adenomas we have seen unilateral, also bilateral, central field defects. In a noteworthy case, visual field charts which the patient brought with him had localizing value, indicating chiasmal involvement. Because we charted centrocecal scotomas and because roentgenograms showed nothing abnormal, we temporized. Later our charts indicated sharply marginal bitemporal defects, and operation revealed a suprasellar meningioma. Finally, demyelination occasionally produces a lesion in the chiasm which results in symmetrical field defects that strongly suggest tumor.

Normalcy of the optic discs in the presence of loss of vision of long duration (for two or three months or longer) strongly suggests extrinsic tumor involving the optic nerves or chiasm. With optic neuritis, almost always pallor of the disc or discs develops a month or two after the onset. In my experience, normal-appearing optic discs have been observed more often with craniopharyngiomas than with any other tumor. I have seen discs which appeared to be normal in cases of pituitary tumor. Curiously, although loss of vision in such cases may have been present for many months or a year or more, the normal-appearing discs before operation have invariably become pale within a few weeks after operation has been performed and the tumor removed.

It is quite impossible to differentiate between optic nerve tumors and chiasmal tumors in any study. It is of interest that in our experience, intrinsic tumors of the optic nerve and of the chiasm occur about equally. In the instance of chiasmal involvement, bitemporal hemianopsia is a standard characteristic feature. We have seen in several intrinsic chiasmal tumors a vertical nystagmus. This has invariably occurred in cases in which the tumor has been rapidly growing, and this is unusual in gliomas of the optic nerve and chiasm.

Other considerations which have a bearing on the differential diagnosis, such as roentgenograms, spinal fluid examinations, injection of air, and arteriography, are not considered here.

TREATMENT OF OPTIC NERVE AND CHIASMAL TUMORS

Excepting metastatic tumors, all others which affect the optic nerves or chiasm, intrinsic or extrinsic, require surgical investigation, and in most instances removal. In regard to orbital tumors affecting the optic nerve, both intrinsic and extrinsic, there has not been unanimity of opinion regarding operative therapy. Some have advised an orbital approach; others have advocated a transcranial approach. The following generalizations seem reasonable.

When there is an orbital tumor present and when there is absence of intracranial extension, the approach should be via the orbit whether the tumor is situated far anteriorly or is in the deep posterior orbit. The exposure effected by various modifications of the Krönlein approach is adequate, and the ophthalmic surgeon is in a position to identify each muscle and remove a tumor with a minimum of trauma. If a similarly adequate field is secured with a transcranial operation, the entire roof of the orbit has been removed. Such a wide removal should be avoided unless a tantalum plate is inserted, or some other plastic procedure is utilized. This is because of the danger of prolapse of the brain into the orbit when wide removal of the orbital roof has been performed. Both with the orbital and with the transcranial approach, the eye may be left in situ. Advocacy of the orbital approach in the instance of deep orbital tumors represents a change from my previous opinion.

When there is evidence of orbital as well as intracranial involvement with tumor (extrinsic or intrinsic), it would seem obvious that a procedure via the transcranial route should be undertaken. The neurosurgeon is primarily responsible. An ophthalmic surgeon may be of great assistance after the orbit has been unroofed.

A combined procedure has been advocated in some cases of retinoblastoma. The optic nerve is cut intracranially, and at a later time the ophthalmic surgeon enucleates the eye and pulls the optic nerve through the canal. I have no proof that this procedure is unsound, but I think that such may be the case.

Roentgen therapy has a definite place in the treatment of optic nerve tumors. When glioma involves the chiasm, roentgen therapy may actually provide improvement in visual acuity. It seems also that life may be prolonged indefinitely. However, since gliomas of the optic nerve and chiasm are characteristically slow-growing, this viewpoint may be unduly optimistic. Surgical removal of gliomas of the chiasm is contraindicated on the basis that it produces blindness, and because of the high mortality associated with such a procedure. Roentgen therapy has some value in metastatic tumors of the eye. Probably this applies in the instances of metastasis to the nerve.

When the optic nerve is removed because of involvement with tumor, it is important not to make the section too close to the chiasm. Such a section accounted for a hemianopic defect in the field of the remaining sound eye in one case which I studied.

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XVI

OPTIC NEURITIS OF UNKNOWN ETIOLOGY

C. Wilbur Rucker, M.D.

For two hours members of this panel have been talking about the various affections of optic nerves, at times with gusto, and always with pretense of authority. If we could stop the discussion at this point, we might be able to leave the impression that we ourselves usually succeed in finding the cause of the disorder and correcting it. Unfortunately, we have had to contend with a chairman who is not only an exacting taskmaster, but one who demands that we be accurate and altogether honest. He insists that we recognize the existence of one last group of disorders of optic nerves, optic neuritis of unknown etiology.

This group is so large as to be embarrassing, for it contains about a third or more of all cases of optic neuritis. In 1952 two large series of cases of optic neuritis were reported: one from the

Eye Institute of New York[2] listed the etiology as unknown in 30 per cent of 240 cases; and a study of 133 cases from Johns Hopkins University[1] recorded 56 per cent as of undetermined etiology. At the Mayo Clinic, efforts to find the cause have failed in about 40 per cent. Passage of time and the later appearances of other symptoms lead finally to a diagnosis in some instances. About half of the young and middle-aged adults who have had optic neuritis will eventually turn up with multiple sclerosis; the other half have no further difficulty, and the etiology remains obscure. Among older persons, the optic neuritis is likely to be ascribed to a vascular disorder.

In a disorder of unknown etiology and variable course, such as optic neuritis, the effect of therapy is difficult to assess. Even the natural course of the untreated disease is clouded, since most patients and their physicians insist on some form of treatment.

During the past half-century undeserved favor has been enjoyed by a wide range of therapeutic measures, which included potassium iodide, sinus surgery, vitamins, foreign protein, histamine and nicotinic acid. There is no convincing evidence that any of these is beneficial, or that they modify the course of the disease in cases of optic neuritis of unknown etiology or that associated with multiple sclerosis. Evaluation of any remedy in these conditions is difficult because of a tendency to spontaneous improvement or recovery, in some instances even after a lapse of one or two years.

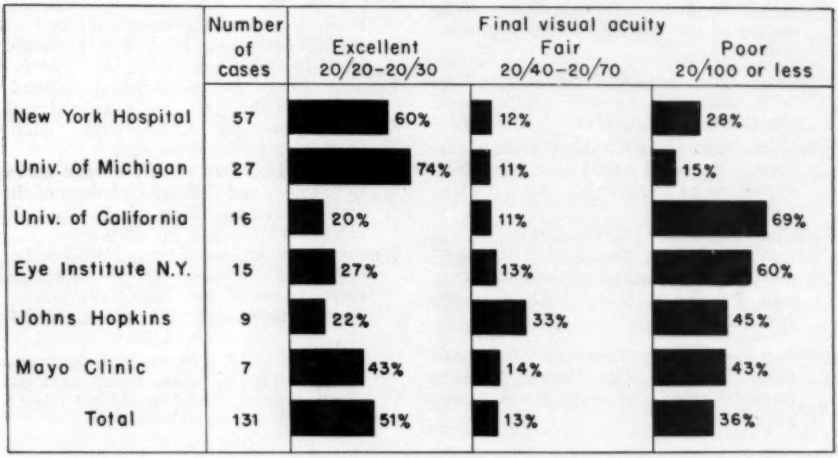

FIG. 1—Cases in which neuritis was treated with corticotropin or cortisone (all causes).

During recent years the efficacy of corticotropin (ACTH) and cortisone has been tested in the treatment of optic neuritis. Information concerning a series of patients treated by this means at New York Hospital has been placed at our disposal by Dr. E. W. D. Norton, and we have obtained data on several other smaller groups treated similarly. The results are summarized in figure 1. At New York Hospital, of the 57 cases of optic neuritis of various etiologies treated with corticotropin, 60 per cent recovered excellent vision. At the Uni-

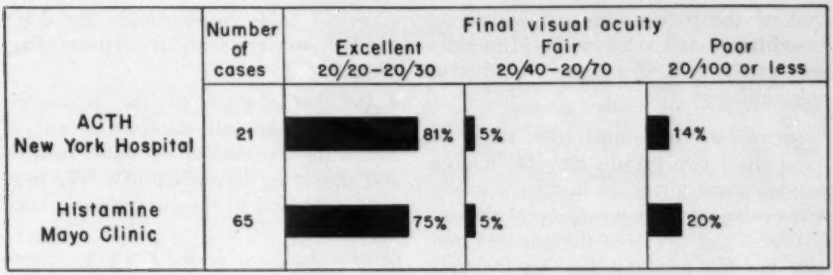

FIG. 2—Results of treatment with corticotropin and with histamine of optic neuritis due to multiple sclerosis.

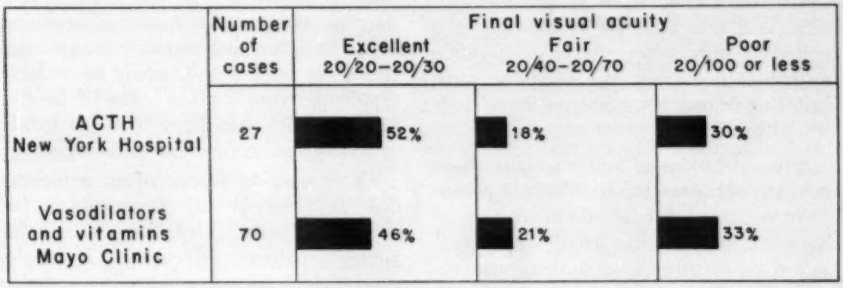

FIG. 3—Results of treatment wih corticotropin and with vasodilators and vitamins of optic neuritis of unknown etiology.

versity of Michigan 27 patients were treated with corticotropin or cortisone, with recovery of vision graded as excellent in 74 per cent. The information that has been made available to us from a number of other institutions consists of smaller groups of cases, in none of which was the response impressive. The apparently superior efficacy of corticotropin and cortisone at the University of Michigan is unexplained. When all these cases are combined, of the total number, about half recovered excellent vision.

As Norton's cases from New York Hospital comprised the largest group and had been carefully tabulated for us, we selected them for special evaluation. Of his 57 cases, 21 were attributed to multiple sclerosis (fig. 2). Through the courtesy of Dr. Henry P. Wagener, we obtained pertinent data on 65 cases of the same variety in which histamine had been used in treatment at the Mayo Clinic. The end results were similar.

Of the New York Hospital series, 27 cases were of unknown etiology (fig. 3). In order to obtain a group for comparison, one of the residents in ophthalmology at the Mayo Clinic, Dr. Fred C. Sabin, reviewed the 378 cases of optic neuritis seen there during the years 1950 to 1954. He found 70 cases of undetermined etiology, in which the patients had not received histamine, corticotropin or cortisone, but had been treated with mild vasodilators and vitamins, and had been followed long enough to ascertain the eventual vision. (Many of the other patients had come only for diagnosis and had returned for care to their local oculists.) The final visual acuity of the patients treated with corticotropin in New York was excellent in 52 per cent, and

that of the patients treated with mild vasodilators and vitamins in Minnesota was excellent in 46 per cent, a remarkable similarity.

Inexact as the comparative study of these latter two groups may be, it does possess some virtue in that each group was evaluated by a young ophthalmologist who had not seen the patients and who had no personal bias in the outcome. Admittedly, central acuity alone is an inadequate record of the outcome of optic neuritis, but it is simple and specific, and was adopted by Norton as a criterion only after much deliberation with his colleagues. We used the same criterion in order to compare other studies with his.

Five instances of optic neuritis have come to our attention in which improvement occurred during administration of hormone therapy, was partly lost on cessation of treatment, and then was regained when treatment was resumed. The effect appeared too definite to be attributed to chance alone. On the other hand, in six other instances, during the time a patient was receiving hormone therapy for optic neuritis of one eye, the same disease appeared in the opposite eye, and in a few instances loss of vision has continued to progress under treatment.

It may be concluded that corticotropin and cortisone are ordinarily of no greater value than other agents in the treatment of optic neuritis of unknown etiology. The possibility that in exceptional cases they may have value cannot be ruled out. Because of the dangers inherent in their use,[3] they are not recommended as routine treatment.

The desirability of thorough search for the etiology in cases of disorders of the optic nerve is apparent. Even though some of the causative factors, such as multiple sclerosis, are not amenable to treatment at the present time, the physician still holds responsibility for doing his best to arrive at an accurate diagnosis.

Detailed studies of the perimetric fields offer the only satisfactory way of following the course of optic neuritis and observing its vicissitudes. We urge more attention to the charting of visual fields, since from the accumulation of careful studies of individual cases comes progress.

Pathologists need specimens of optic neuritis, especially in the acute phase. Anyone who can obtain such a specimen, preferably one that includes the eye and the entire optic nerve, would be making a splendid contribution, even if he did nothing more than place it in the hands of interested, competent pathologists.

Optic neuritis is not often a vicious disease. Generally the prognosis is favorable. Nearly three fourths of the younger patients affected by it regain good vision. Although there is a definite relationship between optic neuritis and multiple sclerosis, the latter supervenes in only half the cases of optic neuritis, and then oftentimes after a lapse of many years; and it need not become disabling. Optic neuritis among older persons is more frequently on a vascular basis and is more likely to leave a visual deficit than among the young. Now, however, at least one form of vascular disease, temporal arteritis, may be mollified by corticotropin or cortisone, and there is every reason to expect that in the future effective remedies will become available for other forms.

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DISCUSSION

DR. CARROLL: We should like to put Dr. Rucker on the spot here and ask him a few questions and see how many he can answer correctly. You know the rules of this contest? As you can perceive, any help from the audience will be appreciated.

Dr. Rucker, please comment on the efficacy of hyperpyrexia and massive doses of hexamethonium chloride in the treatment of multiple sclerosis.

Dr. Rucker, please comment on the efficacy been used for a long time. We were not able to find statistical evidence that patients treated with typhoid vaccine or vasodilators fare any better than do patients treated by other methods.

DR. CARROLL: Dr. Rucker, what about a condition of acute bilateral papillitis with blindness and no other neurological finding in children?

DR. RUCKER: That type of disorder is the kind that frequently follows some of the exanthematous diseases—measles, for example. Did the patient referred to in this question have measles or any of the virus infections? If the questioner is interested, I might suggest that Dr. Henry P. Wagener reviewed the situation a few years ago in the American Journal of the Medical Sciences (Feb. 1952); he might find this a good reference.

DR. CARROLL: Dr. Rucker, I have a patient whose first episode of multiple sclerosis and optic neuritis occurred while she was pregnant. How can you say that there is no relationship?

DR. RUCKER: In preparing material for this symposium I went over the relationship of pregnancy to multiple sclerosis and to optic neuritis as carefully as I could. The best reference that I was able to find was by Ragnar Mueller, who wrote on multiple sclerosis in the Acta medica Scandinavica some years ago. He reviewed about 800 cases, and discussed the relationship of multiple sclerosis to pregnancy. He pointed out that women between the ages of 18 and 40 are in the age group most subject to optic neuritis; if they are to have three children during their lifetime, they will be pregnant about 10 per cent of that time. Consequently he arrived at the conclusion that one tenth of the cases of multiple sclerosis (and I would add about 1 out of 10 cases of optic neuritis) ought to arise in women during a period in which they are pregnant.

DR. CARROLL: Dr. Walsh, what about the cases of unusual injuries you mentioned but did not describe?

DR. WALSH: I had forgotten about them. There have been many cases in the literature of electric current injuries and lightning strokes. From time to time, injury to the optic nerve is associated with operation on the nose or lacrimal sac. I have seen some of such patients. It has always been my belief that a hand slipped some place during the procedure. At least, the loss of vision seems to have been associated directly with the operative procedure. In those instances the ultimate result has been very bad.

Orbital injections affecting the optic nerve have been reported on very briefly. I should like to make mention of the peculiar fact that many people seem unaware that a stream of water under high pressure or air under high pressure can be a very dangerous agent. The individual to whom I referred, who lost the vision of both eyes as a result of injury, was struck by a stream of water under 500 pounds pressure. He was immediately blinded in both eyes. He had a laceration of the sclera in one eye and an iridodialysis in the other eye. Light perception came back in the eye with the iridodialysis in a week. In the eye that had the laceration of the sclera over the ciliary body, the possibility of sympathetic ophthalmia arose. We decided to leave the eye in situ for a while and, by Heaven's grace, we left it long enough to realize that ultimately it may be the better eye. At last examination vision was 10/200 in it and 15/200 in the other eye.

Another case that I think is most unusual and bears brief recounting is that of a patient of Dr. Archie McCannel. The patient was struck by a stream of air that literally tore one eye from its socket. There was no fracture of the orbit, but there must have been traction on the optic chiasm that produced loss of the temporal field in the remaining eye.

Those were the examples of unusual injuries that I had proposed to tell you about.

DR. CARROLL: Dr. Henderson, if the arterial supply to the papillomacular bundle is so limited, why doesn't the trapping operation in internal carotid aneurysms produce visual loss?

DR. HENDERSON: This question was answered to some extent by Dr. Walsh and Dr. Hedges in 1942 in their excellent article on intracranial aneurysms, in which they

showed that there was considerable collateral circulation to the optic nerve by way of the external carotid branches. More recently there has been further evidence of this collateral circulation by arteriography in cases of carotid thrombosis.

It is very interesting to note, too, that this very good collateral circulation which is present in the pial sheath in the optic nerve, and presumably also in the ophthalmic artery, is such that a series of aneurysm cases that I reviewed recently showed that there was no instance of loss of vision with trapping. Even though the ophthalmic artery had to be directly clipped in one case in order to stop bleeding during the procedure, there was still no loss of vision in that eye.

DR. CARROLL: Dr. Zimmerman, in view of the demyelinating action of multiple sclerosis, what is the explanation of the functional recovery seen in periods of remission?

DR. WALSH: I have been asked about the frequent association of glioma of the optic nerve and of the chiasm with von Recklinghausen's disease. Actually, such an association has been described by Dr. Davies and by Dr. Marshall in about 16 per cent of the cases of reported gliomas and, I presume, other primary tumors of the optic nerve. Dr. Marshall mentioned 16 per cent, and curiously, in those cases to which I have access the percentage is precisely the same.

Glioma of the chiasm, of course, cannot be removed surgically because of loss of bilateral vision and the danger to life. Roentgen therapy of the chiasm has been peculiarly successful in a couple of cases that Dr. Davies and I have seen in consultation.

DR. ZIMMERMAN: That brings up another interesting feature of the pathology of multiple sclerosis: at autopsy more lesions are found than can be matched up with the patient's clinical findings. In the lesions of multiple sclerosis, even though they may contain completely demyelinated fibers, the axis cylinders show relatively little damage. This, I think, is the answer to the question as to whether remissions can occur and why there aren't more clinical manifestations to match all of the lesions. That is, the axons are not completely destroyed.

DR. CARROLL: Dr. Zimmerman, what role do the glial cells play in multiple sclerosis?

DR. ZIMMERMAN: I think the person who can answer that question completely, if and when he answers it, will deserve a Nobel prize. The roles of two of the cells, namely the astrocytes and the microglia are pretty well known. The microglia are scavengers. They come in and remove the damaged myelin. That seems to be their main role. After that first damage is done, astrocytes come to "repair." Astrocytes are to the brain what fibrocytes are to tissues elsewhere. So astrocytes have to form a scar.

But the big question, and the one I think a lot of people are thinking about and are working on, concerns the role played by the oligodendrocytes. Some people believe that the basic pathology of multiple sclerosis may be in the deranged metabolism of oligodendrocytes and that they, in turn, because they are deranged, are unable to maintain the myelin.

DR. CARROLL: The question is: "Will someone on the panel state what specific diagnostic tests should be done for a patient with optic neuritis?"

First, we assume that the correct diagnosis has been made. If there was a sudden decrease in vision of one eye with pain on movement and tenderness to palpation, these symptoms point toward the diagnosis of optic neuritis. But if the visual fields indicate that the field defect stops at either the vertical or horizontal midline, an intracranial lesion is more likely. From what has been discussed this morning, it is obvious that the patient should have a thorough medical and neurological examination: laboratory tests should include a complete blood count, blood serology, and roentgenogram of the skull; spinal fluid examination, in my experience, has seldom been helpful, but the neurologist may request this test. The internist will, I hope, be helped by reviewing the report of this symposium, which has indicated the principal causes of optic neuritis.

THE PROBLEM OF REFLUX ESOPHAGITIS

G. Dekle Taylor, M.D.
JACKSONVILLE, FLORIDA

Esophagitis is the lesion most frequently encountered in the esophagus.[15] The chief function of this musculomembranous tube is to carry food, as the Greek origin of the word indicates. Its mucous membrane lining of stratified squamous epithelium provides a protective coating, and the protection it affords is enhanced by a coating of mucus supplied by the mucous glands of the nose, mouth, pharynx and esophagus. Food passes through the esophagus with such rapidity that there is no need for an absorptive or digestive role. The high degree of susceptibility of this lining to inflammation from prolonged contact with gastric secretions has been demonstrated by animal experimentation[10,19] and confirmed clinically. The well-being of the esophageal mucosa is dependent upon the prevention of gastric reflux by the elaborate and mystery-shrouded sphincter-like action of the cardioesophageal junction.

Describing, in 1935, a "new clinical entity," which he designated peptic esophagitis, Winkelstein[26] noted a relationship between acute esophagitis and peptic ulcer of the stomach and duodenum. He ascribed the inflammation of the esophagus in such cases to the action of pepsin and hydrochloric acid on the mucosa. Regurgitation accompanying vomiting, reflux of gastric contents associated with sliding hiatal hernia, an incompetent cardia following thoracic surgery, and surgical excision of the cardiac sphincter are other causes of peptic esophagitis. The term "reflux esophagitis," introduced by Allison,[1] describes this entity more accurately than "peptic esophagitis," however, and is to be preferred also because it lacks the connotation of association with ulcer of the stomach and duodenum which the adjective "peptic" carries. The timely increase in awareness of and interest in reflux esophagitis reflected in the recent literature is to be encouraged, for study of this disease and experience in dealing with it indicate that its incidence is greater than is generally appreciated.[8,20,22]

TERMINAL PORTION OF THE ESOPHAGUS

Regarding the anatomy and physiology of the terminal portion of the esophagus, there is diversity of opinion. The two crura which form the hiatus for the esophagus arise from the upper lumbar vertebrae. Diverging behind the posterior margin of the central tendon, the crural fibers encircle the esophageal hiatus in sphincter-like fashion (fig. 1). The bend in the esophagus, forward and to the left, is, in Allison's opinion, lassoed and maintained by the right crus of the diaphragm, which hitches it down to the lumbar spine.[1] The split in the muscle fibers of the right crus which forms the esophageal hiatus is tightly reinforced by fibers of the left crus. The sling of muscle fibers supporting the esophagus in front is continuous on each side with the perpendicular fibers of the crus, and these fibers decussate with one another to form a stoutly reinforced raphe. Posteriorly, where the crus splits to form the hiatus, there is less support. At this point pressure from below splits the fibers to increase the size of the aperture. Contraction of the right crus of the

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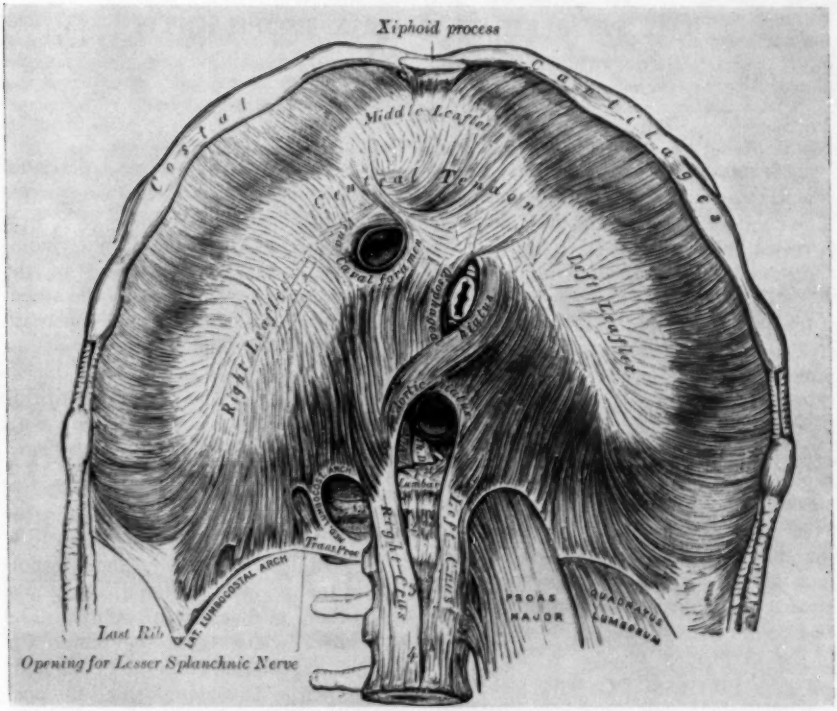

FIG. 1—The diaphragm. (From Gray, Henry: Anatomy of the Human Body, ed. 26, edited by Charles Mayo Goss, M.D., Philadelphia, Lea & Febiger, 1954, p. 453.)

diaphragm compresses the walls of the esophagus from side to side and also pulls down and increases the angulation of this organ from the front backwards and from side to side. During inspiration, with the suction pressure in the chest tending to draw the gastric contents into the esophagus, contraction of the crus of the diaphragm prevents this reflux.

Allison[1] believed that an internal sphincter cannot be demonstrated. He thought that the cardia permits food to pass from the esophagus into the stomach and prevents the reflux of digestive juices from the stomach into the esophagus. It was his belief that an intrinsic mechanism contributes to continence, part of which is the oblique line of entry of the esophagus into the stomach and contraction of the circular muscle fibers of the esophagus and the oblique fibers of the stomach. The contraction of these muscles produces a purse-string action, according to Carver and Sealy,[7] who suggested that air in the cardia has a pressure effect tending to collapse the esophagus and increase the esophagocardiac angle.

Studies by Mosher[12] demonstrated that the anterior or right crus is thin and may be membranous, while the posterior crus is sturdy, making a prominent crease on the posterior surface of the esophagus and notching its left border. He concluded that the terminal

portion of the esophagus varies in form with the changing form of the crural sling. His division of this segment into a vertical and horizontal arm was based on the twist of the esophagus on itself from right to left at the crura of the diaphragm. Observing a close relationship between this portion of the esophagus and the liver, he believed its shape is determined by the liver. It was his conclusion that with the to-and-fro movements of the liver opening and closing the horizontal arm, the patency of this terminal portion is controlled by the position of the liver, and that during the resting state it remains closed because of the pressure in the crural canal, the pressure of the deep vertical folds, and the natural twist to the left. He concluded further that a weak sphincter can be demonstrated occasionally in the lower end of the esophagus and that the musculature there or in the upper end of the stomach has a weak sphincteric action whether or not an anatomic sphincter is present.

His study in cadavers of the closing mechanism between the esophagus and the stomach, believed active in regurgitating stomach contents at the time of death, led Lerche[14] to conclude that a double closing mechanism is effected by structures forming a unit labeled by him the "gastroesophageal segment of expulsion." Roentgen observations in man indicate that a sphincter inherent in the walls of the terminal portion of the esophagus and with a pinchcock action has a role in the closing mechanism.[23]

SYMPTOMS

Substernal pain is usually the initial symptom. Frequently described as heartburn, it is transient and promptly relieved by the ingestion of bland food or antacids; it may radiate to the head, neck, back, or down the arm as in acute coronary insufficiency. As the disease progresses, the pain increases in severity and may persist for several hours, unrelieved by ingestion of antacids or bland food. The patient's description of the pain may be so bizarre as to suggest a functional complaint. Definite clinical symptoms were present in only 10.3 per cent of 213 cases of esophagitis reported by Butt and Vinson.[6] In the series reported by them, the commonest symptoms were substernal burning and pain, hematemesis, and dysphagia, with obstruction a late symptom. Substernal pain, nausea, regurgitation, vomiting, dysphagia, aphagia, hematemesis and melena, occurring singly or in various combinations with progressive stages, were the symptoms observed by Carver and Sealy.[7] Dysphagia results from muscle spasm and edema as the disease progresses, and ulceration later occurs, with resulting fibrosis, cicatricial stenosis, and shortening of the esophagus. Anemia and loss of weight are not uncommon, for patients soon find that they can ingest only liquids, and they refuse to eat because they dread swallowing. Consumption of solid food involves the risk of complete obstruction. In the series of cases recently reported by Stewart, Chardack and Alfano,[20] many patients had had extensive treatment for occult anemia before the diagnosis of reflux esophagitis was made.

DIAGNOSIS

Prompt and proper evaluation of such vague symptoms as fullness in the chest and choking sensations associated with retrosternal burning is important in the diagnosis of reflux esophagitis. They should not be dismissed as mere functional complaints. In the differential diagnosis, angina pectoris, cholecystitis, peptic ulcer of the stomach or duodenum, carcinoma of the esophagus or stomach, true cardiospasm, and peptic ulceration of the thoracic stomach are to be considered.

After a carefully taken history is obtained, roentgen examination of the gastrointestinal tract should follow. With the patient in the Trendelenburg position, cardioesophageal reflux is demonstrated by regurgitation of barium from the cardia into the esophagus, but reflux esophagitis is not present in all such instances. Spasm of the esophagus, irregularity of the mucosal contours, and stenosis may also be observed roentgenographically in reflux esophagitis. In addition, in peptic ulcer of the esophagus secondary to reflux esophagitis an ulcer crater niche may be demonstrated.

The commonest finding roentgenographically in this disease is hiatal hernia,[3] and the roentgen diagnosis of this condition and of a shortened esophagus is important. In order to establish positive evidence of hiatal hernia it is necessary to demonstrate that reflux and filling of the hiatal hernia are spontaneous from a barium-filled stomach. To do so, the stomach is filled with barium and the patient is placed in the Trendelenburg position to produce reflux of barium into the hiatal hernia.

When there is roentgen evidence of esophagitis, esophagoscopy should be performed. Likewise, when esophageal symptoms persist without this evidence, esophagoscopic examination is indicated. To differentiate stricture formation from carcinoma in the late stages of reflux esophagitis, repeated esophagoscopies and biopsies may be necessary, and the specimen for biopsy should be taken from the deep layers of the esophagus. The mucosa is diffusely edematous and inflamed in acute reflux esophagitis, and small ulcers with whitish exudate may be present. In the early stages esophageal spasm may or may not occur; in the later stages stricture formation results in pronounced narrowing of the lumen. Manipulation of the usually friable mucosa readily results in bleeding. When a shortened esophagus accompanies a hiatal hernia, the frequently associated incompetence of the cardia facilitates the entrance of the esophagoscope into the stomach. In cases of this type the usual bending and narrowing of the lower portion of the esophagus are absent.

As Cranmer[8] recently observed, the symptoms of esophageal lesions are frequently attributed to diseases of the heart, lungs, stomach and gallbladder, to which they may be secondary. Consequently, pathologic changes in the esophagus have often been overlooked or neglected. A recent case illustrates some of the problems of differential diagnosis.

REPORT OF CASE

Case 1—A white man, aged 48 years, was hospitalized in April 1955, complaining of dysphagia, burning substernal pain, and vomiting of blood the day prior to admission. One week earlier, after ingesting a small amount of oyster stew, he had felt weak and nauseated and had vomited a mouthful of bright red blood, later that day vomiting a small amount twice. Stools were tarry for three or four days following this episode. He had experienced no hematemesis or melena previously. Ten days, and again four days, prior to the hematemesis, however, he had had a dental extraction, but there was no oral bleeding at the time of the hematemesis.

Eight years previously, vague abdominal pains led to a diagnosis of "ulcer," unconfirmed on roentgen examination. Since then he had been nervous and tense, and for eight months prior to admission had experienced daily choking and burning sensations in the midsternal region, with pain radiating to the shoulders in the early morning but subsiding with breakfast. During this period he suffered from "heartburn" throughout the day; it was worse when he was in the reclining position and was relieved by amphogel. Frequently food seemed to lodge in the lower sternal area, and he would wash it down with water. A full feeling in the chest at times was relieved by vomiting mucus. Anorexia had been present for several months, and he had lost about 25 pounds in weight.

On physical examination, the abdomen was soft and no masses were palpable. The examining gastroenterologist attributed the symptoms to spasm of the cardia, and his differen-

tial diagnosis was (1) duodenal or gastric ulcer, (2) hiatal hernia with esophagitis, (3) esophageal carcinoma, or (4) gastric carcinoma. Urinalysis gave negative results. Examination of the blood disclosed a hemoglobin estimation of 75 per cent (12.5 gm.) with a hematocrit reading of 36, white blood cells 9,300, and a normal differential count. An electrocardiogram was within normal limits.

Roentgen examination of the upper part of the gastrointestinal tract gave only negative evidence. The esophagus and stomach appeared normal; the duodenal cap was smooth and symmetrical, showing no deformities or ulcer crater. Because the gastroenterologist questioned a flattening along the lesser curvature of the stomach, the roentgenologist repeated the examination two days later, but after detailed study it was concluded that there was no indication of a tumor in this region. No cause for the bleeding could be detected.

On the tenth hospital day I was consulted. Complete otorhinolaryngologic examination gave negative results. Because the symptoms were highly suggestive of reflux esophagitis with relaxation of the gastric cardia, esophagoscopy was performed on April 26. A whitish granular surface, which bled rather easily when manipulated, was present throughout the upper third of the esophagus, was less apparent in the middle third, and was more prominent in the lower third. The gastroesophageal junction was so constricted that it was impossible to enter the stomach with a 9-53 esophagoscope or to advance the esophagoscope over the no. 14 French Jackson dilator which was introduced into the stomach. No suspected tissue was seen for biopsy. My diagnosis was reflux esophagitis. The following day the patient was discharged from the hospital.

A regimen of two-hour feedings of milk and an antacid was prescribed, as were also an antispasmodic, an ulcer diet, and a large glass of water after each meal. The patient was requested not to lie down after meals, and the head of the bed was elevated at night to prevent nocturnal gastric reflux. Two months later he felt considerably improved. The sensation of food lodging in the midsternal area was gone, but the substernal burning persisted. He now complained of pain, pleuritic in type, on the left side with tenderness over the left costal margin and postaxillary line. Upon examination of the patient after a cleansing enema, the attending gastroenterologist noted fleetingly a mass in the left upper quadrant of the abdomen, which he believed was in the stomach. Roentgenograms demonstrated a rapid emptying of the stomach, the walls of which appeared rigid.

On June 26, the patient was readmitted to the hospital. General physical examination gave negative results except for a palpable nontender mass in the left flank and left upper quadrant of the abdomen. Urinalysis gave negative results, but pyelograms demonstrated a nonfunctioning left kidney and a severe hydronephrosis on the left side. The urologist who operated on July 1 found the left kidney frozen into position and an indurated mass involving the medial portion and the renal pedicle, which bound down the ureter for a distance of 6 to 7 centimeters. The ureter was freed, and urine was felt to pass this area. A mass was palpable through the peritoneum. The stomach felt leathery to touch, and a mass was palpable in the duodenum. The biopsy report on perirenal tissue was metastatic carcinoma suggestive of metastasis from the lesion in the stomach.

Exploratory laparotomy by a general surgeon on July 20 disclosed a far advanced carcinoma of the stomach with retroperitoneal metastases. The stomach was thoroughly infiltrated, thick and leathery from the esophagus down to within the proximal 1.5 inches of the pylorus. The report on the wedge-shaped portion of the stomach and the distal end of the growth excised for biopsy was diffuse carcinoma in the walls of the stomach. The patient is experiencing a gradual downhill course.

This case illustrates well the signs and symptoms of reflux esophagitis occurring in association with carcinoma of the stomach. My difficulty in passing the esophagoscope to the stomach probably was due to the deeply infiltrating carcinoma without involvement of the mucosa. The long-standing history is noteworthy, and it is probable that the gastric reflux causing the esophagitis was present over a period of years.

PATHOLOGY

Patchy, superficial erosion, surface exudate, and hyperemia characterize early acute ulcerative esophagitis. In almost all cases the distal portion of the esophagus is affected, and in about two thirds of cases this segment alone is involved. The incidence of esophagitis in the esophageal specimens of 3,032 necropsies examined by Butt and Vinson[6] was 213

cases, or 7.02 per cent, and in 76.5 per cent of these cases the lesions were of the acute ulcerative type. Denudation of the lining epithelium was present. Mild to severe inflammatory reaction involved the submucosa and both layers of muscle. In 31 cases, or 14.5 per cent, denudation of the epithelial layer and infiltration with leukocytes gave evidence of a subacute process. Replacement of most of the muscularis mucosae and submucosa with fibrous tissue indicated a chronic process in 14 cases, or 6.5 per cent.

Chronic ulceration, fibrosis, and benign stricture formation mark the progressive course of untreated ulcerative esophagitis. So deeply may the inflammatory change penetrate the walls of the esophagus that stricture with resultant dysphagia may occur within a month or two after the onset of the inflammatory process.[24] In the esophagus, as in the stomach and duodenum, bleeding and perforation may be complications.

ETIOLOGY

In infants, regurgitation of gastric contents occurs normally. Strengthening of the muscles of the diaphragm with age contributes to normal functioning of the closing mechanism of the cardioesophageal junction. In one out of every six infants, evidence of acute esophagitis, usually with ulceration, was noted by Gruenwald and Marsh[11] in their study of 310 autopsies in infants. They thought that obstetric complications and severe asphyxia predispose an infant to esophagitis. Five of six infants with kernicterus had esophagitis. The vomiting of blood by an infant strongly suggests a diagnosis of esophagitis.

Spasm and fibrosis of the circular muscle fibers produce stenosis, and a spasm or fibrosis of the longitudinal muscle fibers shortens the esophagus, thus impairing the function of the cardiac sphincter. In expressing this view, Beaconsfield[3] described a vicious circle of inflammation, fibrosis, constriction, and contraction producing stricture and shortening of the esophagus, drawing the stomach up into the thoracic cavity and increasing the size of the hiatal hernia. This process favors regurgitation of the gastric contents into the esophagus.

There is frequent mention in the literature of the close relationship between esophagitis and other diseases of the gastrointestinal tract. This association is especially noteworthy in those diseases in which frequent vomiting or regurgitation of gastric secretions is a feature. The act of regurgitation and the mechanical factors of stretching may cause small lesions in the esophageal mucosa which tend to produce congestion and erosion of the membrane when bathed by gastric secretion.[13]

Selye[19] established the fact that prolonged contact between the esophageal mucosa and gastric juice results in inflammation by ligating the pylorus in animals and thereby producing hemorrhagic esophagitis. In their animal experimentation, Ferguson and his coworkers[10] also demonstrated the devastating effect of this contact, regarded peptic activity as the important factor, and concluded that preventing reflux of gastric juice into the esophagus should be the objective of preventive measures and treatment in ulcerative esophagitis.

Trauma to the esophageal mucosa by indwelling feeding and suction tubes may make it more vulnerable to the reflux of gastric juice. In addition, the indwelling tube may encourage gastric reflux by partially straightening the twist of the lower portion of the esophagus.[4,6,17] Relaxation of the cardioesophageal orifice at the time of surgery, with resultant bathing of the lower portion of the esophagus with gastric juice, is also a suggested etiologic factor in esophagitis. Another is lymphatic spread of

infection to the esophagus, lowering the resistance of the esophageal mucosa to gastric reflux.

Winkelstein, Wolf, Som and Marshak[27] recently suggested that gastric reflux into the esophagus may result from hypersecretion associated with duodenal ulcer or from an unexplained decrease in the tone of the cardiac sphincter. Duodenal ulcer was present in one third of the 60 cases of benign stricture of the esophagus associated with reflux esophagitis that were reported by Benedict and Sweet.[5] Relief from esophagitis and esophageal obstruction following gastric resection for ulcer was reported by Wangensteen and Leven.[25] Regarding esophagitis as a probable manifestation of ulcer disease, these authors were of the opinion that the esophagus instead of the duodenum would be the commonest site for ulcers if it received all of the gastric juices as does the duodenum. Because of the increased secretion of gastric juice and greater liability of gastric reflux, even in the absence of pyloric stenosis, the ulcer diathesis predisposes to the development of esophageal stenosis, in the opinion of Benedict and Gillespie.[4] They suggested that in patients with an ulcer diathesis, changes may take place in the mucosa of the lower portion of the esophagus which makes it less resistant to acid peptic action. There was evidence of ulceration in the duodenum in 19 of 50 cases reported by Sweet, Robbins, Gephart and Wilkins[21] in which reflux esophagitis with complications necessitated surgery.

Hiatal hernia as a causative factor in reflux esophagitis is emphasized by the frequence of its presence. Esophageal hiatal hernia, either of the short esophagus or the sliding type, was an associated finding in 158 of 170 cases of reflux esophagitis reported by Schmidt.[18] The role of sliding hiatal hernia in the series of Stewart and his associates[20] is indicated by its presence in 42 of their 66 cases of reflux esophagitis. Hiatal hernias occur most often in the fourth decade of life and later, when the tissues about the hiatal orifices are relaxed. Increased intra-abdominal pressure may be a factor. Reflex shortening of the esophagus in the experimental animal with the production of esophageal hiatal hernia due to traction upon the stomach by electrical stimulation of the vagus nerve, or reflexly from stimuli originating in the viscera of the upper part of the abdominal cavity, has been demonstrated.[9]

The two types of hiatal hernia, paraesophageal and sliding, may exist separately or in combination. A paraesophageal hernia is a herniation of the stomach through a preformed peritoneal sac, always situated anterior to the hiatus. In some persons a protrusion of the peritoneal sac may remain in the hiatus. The hernial sac may remain empty during the patient's entire life, according to Allison,[2] or at any age a part of the anterior surface of the stomach may project into it. It is possible for the hernial sac to fill only by the rolling up of the anterior wall of the stomach, provided the ligaments of the cardia remain strong. In paraesophageal hernia, the esophagus still enters the stomach at an acute angle, and a dilated stomach, when filled, lies between the pericardium and the spine. Thus the esophagus is compressed from the front backward, and regurgitation of gastric contents into it is prevented. Patients with this type of hiatal hernia do not develop esophagitis, but they may complain of shortness of breath and fullness after meals.

In the sliding type of hernia, general weakness of the muscles and ligaments at the cardia permits the acute angle between the esophagus and the stomach to disappear, and the cardia slides up into the mediastinum. During the early phase,

when the esophagus appears shortened because of its elastic recoil, it is only relaxed and may be pulled back into its normal position by slight traction of the stomach at operation. The mechanism characterizing paraesophageal hernia, which normally prevents gastric reflux, no longer exists in this type of hernia. In many cases peptic esophagitis develops because of the reflux of gastric contents into the lower portion of the esophagus. In the early stage, cure is effected by a simple reduction of the hernia, as advocated by Allison.[2]

The advanced stages of esophagitis, including chronic ulceration and stenosis, result when the sliding hernia persists. With continued progression of the disease after the hernia is no longer reducible, resection of the esophagus may become necessary.[2] When there is a congenitally short esophagus, a condition believed to be rare, esophagitis similar to that associated with the sliding type of hernia may occur. Doubtless in many instances the condition previously diagnosed as congenitally short esophagus represents the sequence described by Allison,[2] in which the shortened esophagus is secondary to the loss of elastic recoil with subsequent maintenance of the retracted position due to formation of scar tissue.

Operations for cardiospasm and benign stricture of the esophagus, performed now with increasing frequency, too often result in an incompetent cardia, permitting regurgitation of gastric contents into the lower portion of the esophagus, with eventual development of reflux esophagitis. Dilatation remains the time-honored treatment of choice, with surgical correction serving as a last resort. The incidence of reflux esophagitis has increased for the same reason, because of the frequency with which esophageal resection for malignant disease is now performed. In their series of 65 cases in which esophagogastrostomy or cardioplasty was performed, Ripley, Olsen and Kirklin[16] reported subsequent evidence of reflux esophagitis and formation of stricture in 28, and presumptive evidence in 12. They commented upon the need for developing techniques to prevent this sequela. Sweet and his associates,[21] however, stressed a 90 per cent rate of satisfactory clinical results if the operative procedure for peptic ulcer and stricture of the lower portion of the esophagus is wisely chosen to suit the conditions encountered in the age and physical status of the patient.

Care should be taken to watch closely for symptoms of reflux esophagitis in cases of esophageal resection and anastomosis with the stomach and jejunum. Such prophylactic measures as sleeping with the head of the bed elevated and the use of antacids for substernal discomfort should be instituted. When symptoms are definite, esophagoscopy is indicated.

Cases 2 to 8, previously reported,[22] are here briefly reviewed, and case 9 is reported to illustrate various causative factors in reflux esophagitis.

REPORT OF CASES

Case 2—Esophageal Stricture Associated with Long-Standing Duodenal Ulcer. In August 1950, a 59-year-old white man complained of dysphagia, substernal distress, and a sensation of food stoppage under the lower third of the sternum of several weeks' duration. He reported frequent attacks of nausea, vomiting and epigastric pain relieved by feedings since diagnosis of a small duodenal ulcer in 1941. Such an attack was especially severe in March 1950 and was accompanied by hemorrhage from the ulcer. Roentgen examination in August of that year gave evidence of esophagitis and an active duodenal ulcer. The patient refused esophagoscopy. In October, he experienced five bouts of severe hemorrhage from the duodenal ulcer. When a piece of meat caused complete obstruction of the esophagus in January 1952, roentgenograms showed narrowing of the lower third of the esophagus

with impaction of food. Diagnostic esophagoscopy was again refused. In November, a massive hemorrhage necessitated subtotal gastric resection, and a chronic constricting duodenal ulcer showing active bleeding was found.

Always high strung and hard-working, the patient experienced increasingly severe symptoms of substernal burning and food blocking the midesophagus in June 1953, especially when he was under emotional stress. The following month, esophagoscopy revealed an orange seed causing complete esophageal obstruction 40 centimeters from the incisor teeth, mild inflammatory change in the mucous membrane at the site of the stricture, and pronounced narrowing below it. Dilatations were begun with a no. 18 French Hurst dilator and were continued until October, when a no. 30 French dilator was the largest that could be passed. Although occasionally the patient still has difficulty swallowing solid foods, he has had no further dilatations, and by eating slowly and chewing his food thoroughly, he gets along well.

Case 3—Reflux Esophagitis Associated with Vomiting of Pregnancy and Duodenal Ulcer. A white woman, aged 63 years, consulted me in July 1953, complaining of dysphagia with food seeming to lodge in the mideosophagus, pain radiating to the throat, shoulder and hand on the right side, and intermittent pain in the epigastrium on the left side, especially when she was nervous or upset. Frequently, unpredictable bouts of substernal burning lasted from several hours to several days. Severe vomiting during pregnancy in 1933, with vomiting of blood two or three times daily for two weeks prior to delivery, marked the onset of symptoms. Several days after a normal delivery the vomiting ceased. Progressive dysphagia began three weeks later, and within one month she was unable to swallow water. Her physician in Philadelphia reported several esophagoscopies and dilatations over a period of five years for a peptic ulcer in the lower third of a short esophagus and ulceration at the junction of the esophagus and stomach.

Thereafter, she experienced dysphagia only occasionally until 1948, when recurring dysphagia and vomiting associated with nervousness and tension necessitated hospitalization in New Jersey. Narrowing of the lowermost 5 centimeters of the esophagus, a questionable esophageal ulcer, and a constant slight deformity of the duodenal cap were demonstrated roentgenographically at that time. Esophagoscopy revealed stenosis of the distal third of the esophagus, with some ulceration of the mucous membrane. Dilatations were carried out up to a no. 27 French Hurst dilator.

Recurrent dysphagia led to hospitalization in Florida in 1952 with roentgen diagnosis of moderate cardiospasm without dilatation and a chronic duodenal ulcer. Despite treatment for the duodenal ulcer, dysphagia persisted. Esophagoscopic examination by the patient's New Jersey physician in June 1953 disclosed a narrowing of the distal third of the esophagus with ulceration of the mucous membrane. Attempts at passing bougies were unsuccessful, and the patient was unable to swallow a string. The diagnosis of the physician was esophagitis with cardiospasm and stricture secondary to duodenal ulcer. He referred the case to me.

When the patient first consulted me on June 10, examination of the esophagus by barium swallow was reported as giving no evidence of an intrinsic lesion, dilatation or cardiospasm. Esophagoscopy on August 13 disclosed, just above the esophageal junction, a narrowing of the esophagus with a horizontal shelf on the right side. Beneath this area there appeared to be a stricture with acutely inflammed mucous membrane. The esophagus was dilated until a no. 21 French Jackson dilator could be passed with difficulty, but the following week a no. 18 French Hurst dilator was the largest I could pass. Subsequent dilations were carried out over a string at weekly intervals for three months until a no. 27 French dilator was employed. The dysphagia then subsided. Early in 1955, a no 27 French Hurst dilator was being passed at six-week to eight-week intervals. The patient was on an ulcer diet and taking antacids. Except for some heartburn associated with nervousness, she was asymptomatic. She subsequently returned to New Jersey.

Case 4—Esophagitis Associated with Reflex of Gastric Content Following Cholecystectomy. A 58-year-old white man with a history of dysphagia, indigestion, and flatulence since boyhood had experienced increasing dysphagia associated with pain radiating to the back and right side of the neck since undergoing cholecystectomy seven weeks before consulting me in April 1951. Three weeks postoperatively he could swallow liquids only, and at that time a narrowing of the lower third of the esophagus was demonstrated by barium swallow. Gastric acidity was within normal limits before and after administration of histamine.

Esophagoscopy revealed an acute esophagitis, confirmed on biopsy, and a greatly narrowed lower portion of the esophagus. Two weeks later a diagnosis of nonspecific severe

postoperative esophagitis was made elsewhere, and following gastrostomy there, the patient returned to my care. Weekly retrograde dilatations, begun in July with a no. 34 French Tucker dilator, were discontinued in September. Soon the patient was using a no. 40 French Hurst dilator himself every 48 to 72 hours without difficulty and was experiencing much less dysphagia, although findings on esophagoscopy were much the same in late October. In March 1952 the constant narrowing of the lower portion of the esophagus with dilatation above was demonstrated roentgenographically (fig. 2). After four years of treatment, the patient now experiences no dysphagia. At monthly intervals, or whenever he notices any indication of recurrent dysphagia, he carries out dilatation himself with a no. 40. French Hurst dilator.

FIG. 2—Case 4. Roentgenogram showing constant narrowing of the lower portion of the esophagus with dilatation above in March 1952.

Case 5—Chronic Reflux Esophagitis Progressing to Stricture Formation Following Cholecystectomy Associated with Indwelling Tube and Severe Vomiting Postoperatively. A 64-year-old white woman complaining of dysphagia first consulted me in December 1952, four months after uneventful cholecystectomy. Preoperatively, there was no roentgen evidence of esophageal or gastric abnormality. For four days postoperatively a Levin tube was left in place. Severe and persistent vomiting then occurred and continued intermittently for three weeks. Because of recurrent symptoms of esophageal spasm, examination by barium swallow in mid-September gave negative results, but in late November narrowing and irregularity of the lower two thirds of the esophagus were demonstrated (fig. 3). Gastric acidity, before and after administration of histamine, was within normal limits.

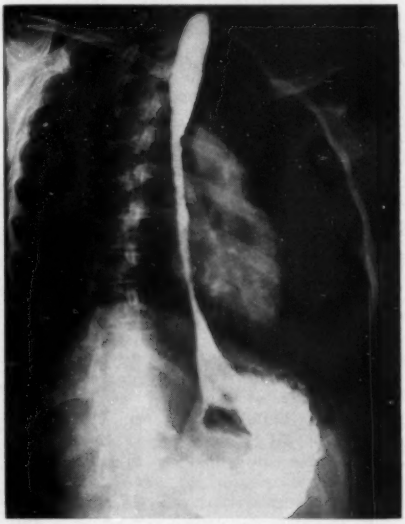

FIG. 3—Case 5. Roentgenogram showing narrowing and irregularity of the lower two thirds of the esophagus in November 1952.

Following esophagoscopy in December, my diagnosis was acute esophagitis with pronounced narrowing of the esophagus. The biopsy report indicated the presence of a granulomatous inflammatory process with necrotic tissue. Six weeks later, dilatation with a no. 16 French Hurst dilator was especially difficult, and in March 1953 gastrostomy was necessary. When retrograde dilatations were discontinued in June, a no. 38 French Tucker carried retrograde dilator was in use, and dilatations from above were easily carried out with a no. 24 French Hurst dilator. In September, gradual narrowing of the esophagus recurred until only a no. 16 French dilator could be used. Since

then, dilatation over a string has been carried out, with the Hurst dilator used intermittently. In March 1954, esophagoscopy demonstrated a markedly narrowed lower portion of the esophagus and acute esophagitis; roentgenograms showed tapering of a 7-inch segment with stricture formation (fig. 4).

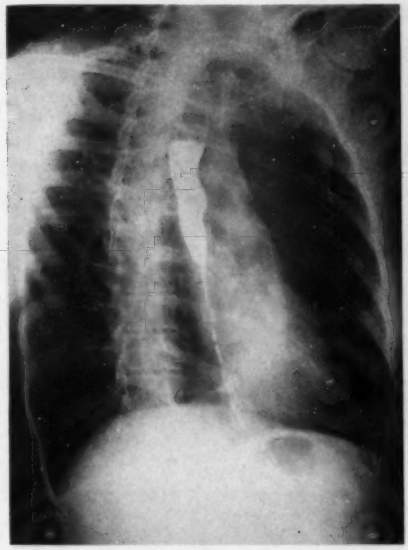

FIG. 4—Case 5. Roentgenogram showing advanced esophageal narrowing in March 1954, 16 months later.

There have been 90 dilatations to date. A no. 22 French dilator is now used every six to eight weeks, as too frequent dilatations of a tight stricture of this type may lead to increased stricture formation because of persistent inflammation incident to local trauma and spasm. The condition appears to be stabilizing, as there is less dysphagia than at any time. The patient refuses to consider possible surgical alleviation.

Case 6—Reflux Esophagitis Secondary to Esophageal Surgery for Carcinoma. A white woman, aged 50 years, consulted me in June 1950 because of progressive dysphagia of three months' duration. Roentgen examination demonstrated an irregularity of the lower portion of the esophagus, and esophagoscopy revealed a raised ulcerated lesion in this area. The biopsy report was squamous cell carcinoma.

In July the referring surgeon resected the lower two thirds of the esophagus and performed an esophagogastrostomy above the arch of the aorta. The patient made an uneventful recovery and was able to swallow a soft diet without difficulty. Four months postoperatively she began to experience dysphagia for soft foods. In March 1951 there was roentgen evidence of narrowing of the esophagogastric anastomosis (fig. 5). Esophagoscopy showed the esophagus displaced to the left posteriorly and dilated above the site of the anastomosis, which was so greatly constricted that a no. 18 French Jackson dilator was introduced with difficulty. Retained secretions were present, and the mucosa was inflamed but intact. The dysphagia persisted for three months. After radical dissection of the glands of the neck on the left side in October 1951 for metastatic carcinoma of the supraclavicular nodes, recovery was again uneventful.

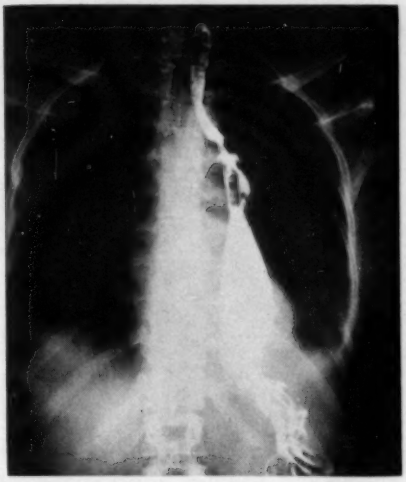

FIG. 5—Case 6. Roentgenogram showing narrowing of the esophagus at the anastomosis with the stomach in March 1951.

In September 1955 there is no evidence of further metastasis, and the patient is able to eat anything but onions and fatty foods.

Case 7—Reflux Esophagitis Following Total Gastrectomy, Splenectomy, and Partial Esophagectomy with Esophagojejunostomy for Esophageal Carcinoma. A 48-year-old Negro woman, complaining of dysphagia, was referred to me in May 1954 after being sub-

jected in March to total gastrectomy, splenectomy, and partial esophagectomy with an esophagojejunostomy for carcinoma of the lower third of the esophagus extending down to the cardia. The lower two thirds of the esophagus was resected and anastomosis with the jejunum made above the aorta. The surgeon noted a poor blood supply of the jejunum at the site of anastomosis.

Six weeks postoperatively there was onset of progressive dysphagia and epigastric pain. In June stricture at the site of the anastomosis was demonstrated roentgenographically (fig. 6), and acute esophagitis from just below the cricopharyngeus pinchcock to the markedly constricted site of anastomosis was observed on esophagoscopic examination. A no. 12 French Jackson dilator was passed through the narrowed area with difficulty. The course of the disease was progressively downhill, and the patient died of generalized carcinomatosis that same month. Microscopic section of the esophagus revealed severe esophagitis but no recurrent neoplasm.

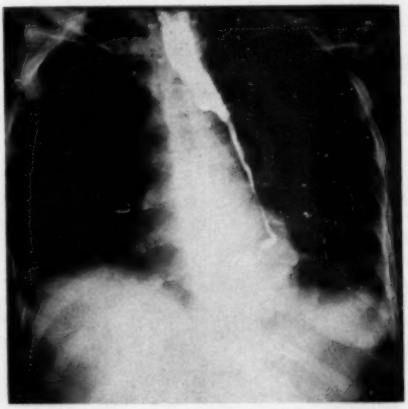

FIG. 6—Case 7. Roentgenogram showing narrowing of the esophagus at the anastomosis with the jejunum in June 1954.

Case 8—Reflux Esophagitis Associated with Hiatal Hernia and Shortened Esophagus. An intense, apprehensive white executive, aged 41 years, referred in February 1950 for esophagoscopy, had multiple complaints, seemingly mostly functional in nature. There was a 16-year history of substernal discomfort, a sensation of food blocking in the midsternal region, and postprandial regurgitation of acid-free food. Cardiospasm frequently had been diagnosed, and esophageal dilatation had been advised.

Roentgen diagnosis on February 6 was esophagitis, hiatal hernia, and possible ulceration of the esophagus. On esophagoscopy five days later, observations were: areas of inflammatory change just above the gastroesophageal hiatus, a wide hiatus opening directly into the stomach from a shortened esophagus with absence of the usual twist in the terminal portion of the esophagus, and gastric mucosa normal in appearance. The final diagnosis was esophagitis, hiatal hernia, shortened esophagus, and severe anxiety state. Attempted dilatation of the esophagus with a Hurst dilator was unsuccessful because of gagging and anxiety. An ulcer regimen brought rapid improvement.

Severe attacks in December 1951 and June 1954, associated with overindulgence in food, necessitated hospitalization. Roentgen diagnosis in 1954 was hiatal gastric hernia and possible ulcer crater of the esophagus. As previously, there was improvement with rest and an ulcer regimen. The substernal discomfort more or less paralleled the expenditure of energy in business affairs. The patient consulted me frequently until June 1954. Recently he stated that the symptoms of choking and substernal discomfort persisted, but since dilatation over a string was carried out elsewhere in August 1955, he has been completely free of symptoms.

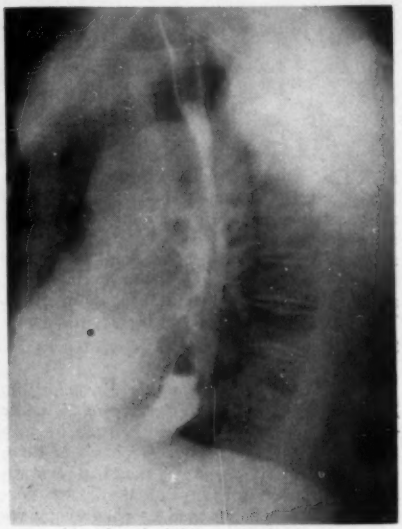

FIG. 7—Case 9. Roentgenogram showing shortened and narrowed esophagus with large sliding hiatal hernia in September 1954.

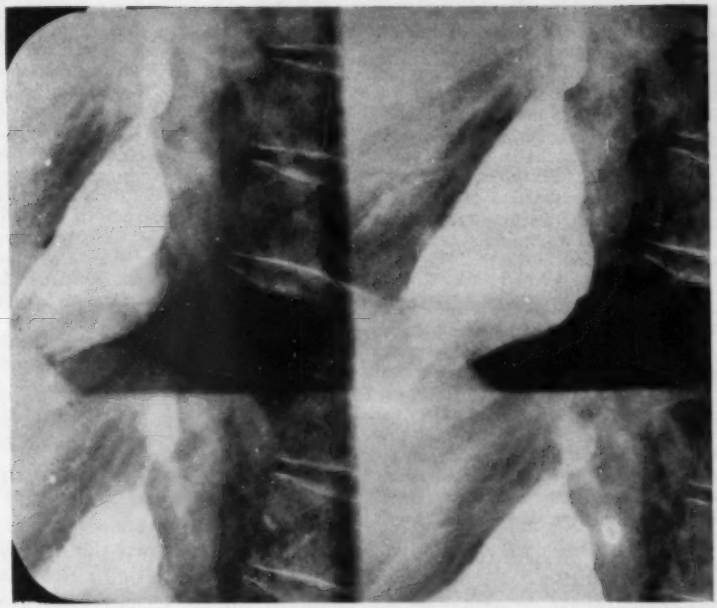

FIG. 8—Case 9. Spot films showing junction of narrowed esophagus and sliding hiatal hernia in September 1955.

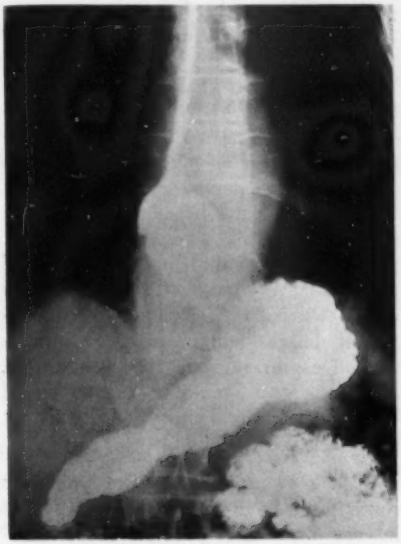

FIG. 9—Case 9. A no. 18 French Hurst dilator passed with ease through the area of esophageal narrowing into the herniated gastric pouch.

Case 9—Reflux Esophagitis Associated with Hiatal Hernia and Shortened and Narrowed Esophagus. A white man, aged 75 years, complained on September 20, 1955, of difficulty in swallowing and "heartburn." For approximately 40 years he had experienced epigastric and retrosternal pain associated with postprandial indigestion. The burning pain started in the region of the xiphoid process and radiated up into the throat. For the last nine years these symptoms had been worse. In 1946, severe precordial and retrosternal pain accompanied by vomiting led to hospitalization in Georgia for six weeks, with vomiting recurring daily. The patient was told that he probably had a coronary occlusion, although the electrocardiogram was nonspecific. Because of persistent vomiting and a severe bout of hematemesis during one week at home, he returned to the hospital for seven more weeks. During that period he vomited daily and had several severe bouts of hematemesis. Examination by barium swallow resulted in a diagnosis of cancer in the late stages, and the man was told there was no treatment.

In 1947, another physician was consulted, and examination by barium swallow resulted in a diagnosis of hiatal hernia, confirmed elsewhere in 1948 and 1949. Dysphagia has per-

sisted since the episodes of vomiting in 1946, as have intermittent bouts of hematemesis every three or four months. The patient has had three blood transfusions in the last year because of hematemesis, and he frequently has vomited small amounts of material resembling coffee grounds. Although he has been able to swallow only liquids for the past three years, he has maintained good nutrition with a well balanced liquid diet and amino acid supplements. Practically all of the time for the past four years he has had a burning sensation in his chest, which is worse in the reclining position.

Examination by barium swallow in September 1954 demonstrated a shortened esophagus with a pronounced narrowing of this organ just above the junction with a large hiatal hernia (fig. 7). Similar roentgen findings existed on September 30, 1955, ten days after the patient first consulted me (fig. 8). During this examination there was no apparent impediment hindering the flow of barium, which rapidly passed through the area of esophageal narrowing into the herniated gastric pouch (fig. 9).

On the preceding day, the results of the general physical examination were within normal limits except that the patient was underweight. On otolaryngologic examination, no abnormalities were noted. The red blood cell count was 4,590,000, and the hemoglobin estimation was 13.6 gm. (87 per cent).

Under local anesthesia an esophagoscopy was performed on October 1. In the upper third of the esophagus retained greenish secretions were present, and a slight amount of whitish exudate was observed on the mucosa. Thirty centimeters from the incisor teeth, there was a definite narrowing involving the entire circumference of the esophagus. For approximately 10 centimeters proximal to this area, the esophagus was markedly inflamed, edematous and covered with a creamy white exudate. This area bled very rapidly with the slightest manipulation. The narrowed portion was dilated with a no. 16 French Jackson dilator. The tissue was not suggestive of a neoplasm, and no specimen was taken for biopsy. A diagnosis of severe chronic esophagitis with esophageal narrowing associated with sliding hiatal hernia was made.

Several hours after the esophagoscopic examination was completed, the patient vomited approximately 100 cc. of bright red blood. During the next 12 hours he vomited about 500 cc. of blood, intermittently raising 50 to 100 cc. of bright red blood and material resembling coffee grounds. The red blood cell count dropped to 3,510,000, with a hemoglobin estimation of 11.8 gm. (76 per cent). The patient received a transfusion of 500 cc. of blood. Hematemesis has not recurred.

On the second day following esophagoscopy, dilatation was easily carried out with a no. 16 and a no. 18 French Hurst dilator. On the next day a no. 24 French Hurst dilator was used. The patient was discharged from the hospital at that time with instructions to keep the head of his bed elevated; an antacid was prescribed for the symptoms of heartburn. On the following day his daughter telephoned to say that he had been able to swallow such soft foods as squash and macaroni for the first time in years. On October 7, dilatation was carried out up to a no. 30 French Hurst dilator without difficulty, and the patient stated that the difficulty in swallowing was much improved.

COMMENT

Vinson[24] estimated that 10 per cent of benign esophageal strictures result from the vomiting of pregnancy. In case 3 the sequence of events probably represented an acute reflux esophagitis following the vomiting of pregnancy, which progressed through the stages of chronic ulceration, fibrosis and stricture. It is likely also that the duodenal ulcer was reactivating the chronic esophagitis from time to time, causing increased stricture formation, esophageal spasm, and symptoms of dysphagia. Particularly noteworthy in this case is the lack of roentgen evidence of esophageal disease in a patient experiencing severe dysphagia. At times, as Vinson[24] observed, the lumen of a stricture is small enough to impede normal swallowing of solid food and yet large enough to permit passage of a thick paste of barium without apparent delay during roentgen examination. Despite normal roentgenograms, esophagoscopy should be recommended when there is a history of persistent dysphagia.

Spread of infection by the lymphatic route might have been a causative factor in case 4. Another possible cause is relaxation of the cardioesophageal orifice at the time of cholecystectomy, thus per-

mitting bathing of the lower portion of the esophagus with gastric juice.

The persistence of the inflammatory activity in case 5 is noteworthy. Probably it was due to continued gastric reflux into the inflamed esophagus because of impaired function of the terminal portion of the esophagus.

That reflux of intestinal juice is also capable of causing a reflux esophagitis is suggested by case 7.

Case 9 illustrates well the symptoms and progressive steps of esophagitis accompanying untreated sliding hiatal hernia. Had the disease been recognized earlier and the hiatal hernia repaired, the shortening of the esophagus and stricture probably could have been prevented.

TREATMENT

Most patients with symptoms of reflux esophagitis respond to conservative management provided the diagnosis is made before the disease has progressed to the more advanced stages. The use of antacids, antispasmodics and good oral hygiene is of value. To prevent nocturnal gastric reflux, the patient should sleep with the head of the bed elevated, even after symptoms have subsided.

Carver and Sealy[7] advocated three large liquid or semisolid feedings daily to decrease esophageal peristaltic activity, a glass of water after each meal to clear food particles from the lower portion of the esophagus, and a liquid antacid to be taken at the first indication of substernal discomfort and at night before retiring. Atropine administered thirty minutes before meals reduces spasm and gastric secretions. For spasm and early stenosis, gentle bouginage may be carried out. Carver and Sealy[7] favored continuing treatment until the patient is free of pain for at least two weeks, three consecutive stools show no occult blood, and roentgen studies give no evidence of an ulcer crater or delay of barium passage through the lower third of the esophagus. For two or three months after subsidence of symptoms, a bland diet should be taken.

In patients with sliding hiatal hernia, Allison[2] believed repair of the diaphragm should be carried out before shortening of the esophagus occurs. This measure prevents the progressive phases of reflux esophagitis by restoring the normal cardioesophageal mechanism.

Chronic ulceration and stricture, manifested by dysphagia, require a program of bouginage in addition to conservative treatment. For this purpose, dilatation over a string with olive-tipped bougies is the most satisfactory procedure. Hurst mercury-filled bougies may be used later when there is sufficient dilatation. It may be necessary to resort to temporary gastrostomy and retrograde dilatation in severe cases. Gastrostomy permits the esophagus to be at rest and also provides for maintenance of adequate nutrition.

In cases of ulcer or stricture of the esophagus with a history of bleeding, obstruction unsuccessfully treated by bouginage, intractable pain, and sometimes perforation, Sweet and his associates[21] advocated such surgical measures as a limited esophageal resection with end-to-end anastomosis, esophagoplasty, and partial esophagectomy and gastrectomy with an esophagogastroanastomosis. When esophageal ulcer, hiatal hernia and duodenal ulcer are present, Carver and Sealy[7] regarded subtotal gastric resection with repair of the hiatal hernia as the treatment of choice. The therapeutic value of gastrectomy for the relief of esophageal obstruction secondary to ulcer disease lies in the reduction of the acidity and digestive capacity of the gastric juice and shortening of the gastric emptying time, in the opinion of Wangensteen and Leven.[25]

Although theoretically justified as a means of reducing the volume of gastric secretion, gastric resection in cases of esophageal stenosis and duodenal ulcer is not established as a prophylactic or curative measure at present, in the opinion of Benedict and Gillespie.[4] They have added in their report that repair of a hiatal hernia which causes symptoms and does not respond to other therapy is desirable, but that the value of a repair operation as a prophylactic measure has not been proved.

SUMMARY

Familiarity with the closing mechanism of the esophagocardiac junction is essential to the understanding of reflux esophagitis. Impairment of its function allows reflux of gastric contents with a high acid pepsin concentration to have a corrosive effect on the esophageal mucosa. This action is particularly harmful to the nonresistant squamous mucosa of the terminal portion of the esophagus, causing an acute erosive esophagitis to develop, which progresses, if untreated, to acute ulcerative esophagitis with subsequent destruction of the muscularis coat and cicatricial stenosis of the esophagus. Prompt recognition of the early symptoms is therefore important if these progressive stages of the disease are to be avoided. These symptoms may readily be mistaken for functional complaints.

The role of the terminal portion of the esophagus in reflux esophagitis is described, and the symptoms, diagnosis, pathologic changes, causative factors, and treatment, both medical and surgical, of this disease are discussed. Particular emphasis is placed upon etiologic considerations, with eight illustrative cases described. A case also is reported which portrays various aspects of the problem of differential diagnosis.

The importance of esophagoscopy in the diagnosis and understanding of this disease is stressed.

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DISCUSSION

WALTER H. MALONEY, M.D., Philadelphia: The confusion which arises from the clinical similarity of diseases of the gastrointestinal, respiratory, nervous and circulatory systems can be lessened if one keeps in mind the developmental anatomy of these systems.

(Slide) These systems develop simultaneously in the embryo. The three-to-twelve-week stage is the crucial one, and it is at this time that any interruption of differentiation may result in anomalies of one or more of the various systems.

If one recalls the early relationship of the foregut, lungs and heart to the medulla oblongata and vagus nerve, the inter-relationship of normal and abnormal visceral reflexes in the adult (slide), for example, respiration, phonation, circulation, secretion, and peristaltic movements, becomes more logical and more easily understood. But most important, the proper differential diagnosis is foremost in your mind when a patient is sent to your office complaining of nausea, vomiting, dysphagia, vertigo, heartburn, and numerous other related visceral pains.

That this problem of reflux esophagitis is very real can best be illustrated by three cases which I drew from my service at Hahnemann Medical College and Hospital. We are cooperating in a research problem on denervated heart. This requires bilateral vagotomy and sympathectomy, among other things. But immediately the problem of regurgitating and vomiting, resulting in eventual death, occurs. (Slide) This slide, showing the ulceration of the esophagus with perforation and herniation of the stomach through it, serves to illustrate the terrific ulcerative action of the gastric juices on the esophagus when the normal neurophysiology of the esophagus and stomach was interferred with.

(Slide) The next case is one of a 61-year-old white male who complained of dysphagia for two years following a long period of coma and tube feeding, which were part of the complication, and treatment of a severe ulcerative colitis and diverticulitis. I feel that the stenosis and esophagitis are results of regurgitation of gastric juice plus the continuous irritation of the feeding tube. This patient has responded nicely to a medical regimen including dilatation of the esophagus, using a string for guidance, followed by Jackson bougies, and finally with Hurst mercury-filled bougies. Such a case illustrates the need for prophylaxis and careful postoperative follow-up to prevent the inevitable sequela of chronic esophagitis, which is cicatrical stenosis.

(Slide) My last case is one of a 40-year-old white female, nervous, anxious, and single, who complained of a lump in the throat and food sticking in her throat during eating. She had no pain and no other complaint. She was a natural for the diagnosis of hysterical dysphagia. However, the roentgenograms revealed a ring-like contraction of the lower esophagus, and esophagoscopy demonstrated a firm stenosis with minimal inflammation of the esophageal mucosa.

Our radiologist has suggested that this is a typical roentgenogram of the so-called lower esophageal ring described by Schatski in the American Journal of Roentgenology in De-

cember 1953. It is, however, very similar to the picture seen in reflux esophagitis with fibrosis and stenosis. Both are in the lower esophageal segment, but the ring is more symmetrical, is quite short, and is not as rigid in contradistinction to the true cicatrical stenosis of reflux esophagitis.

This case fits the picture very well except for the esophagitis noted. I present it to illustrate the difficulty of categorizing these problems and to emphasize the need for complete esophageal work-up, which must include excellent radiography and esophagoscopy for even the most obviously functional complaint.

In conclusion, I would like to congratulate Dr. Taylor for reviewing for us and presenting this very excellent subject of reflux esophagitis. I would recommend it to you for your close study at home.

DANIEL C. BAKER, M.D., New York City: The problem of reflux esophagitis is a large one. In our gastroenterology clinic, of which I am an associate member, we have an increasing number of patients. In 1952, the Departments of Radiology, Gastroenterology and Otolaryngology made specific studies on patients with hiatal hernia. In a short period we had collected about one hundred cases. The results of our studies are shown on the slides.

(Slide) 52 patients with hiatal hernia were given barium to swallow and were studied fluoroscopically in both the upright and Trendelenburg position. Reflux was demonstrated in 24 instances.

The second study was an attempt to demonstrate reflux by aspiration of the contents of the esophagus by means of a small feeding tube. 32 patients with hiatal hernia were placed in the recumbent position and a small tube was introduced into the esophagus above the level of the hernia. It was possible to demonstrate reflux by finding acid in the esophagus in 17 patients.

(Slide) The third study was that of esophagoscopy. This procedure was performed on 22 patients with hiatal hernia. There were 8 patients who had reflux and 4 of these had severe esophagitis.

Probably the reason for the increase in the number of patients who have a hiatal hernia is the fact that we are living longer and arriving at an age when this condition occurs.

I would like to say just one word about the surgical treatment of reflux esophagitis, particularly those cases that have stricture. During the past few years everyone doing esophagoscopy has encountered an ever increasing number of patients with postsurgical stricture. The latter is due to reflux either of gastric contents or in some instances the alkaline contents of the small intestines after surgery has been performed.

This means that when you have a patient who has a hiatal hernia with a stricture or ulceration, and he is difficult to treat, you don't just turn him over to the surgeon, with the idea that the surgeon is going to solve the problem. Unfortunately, after the surgery has been performed, the patient may return to you because he has developed another stricture which requires treatment. I have seen postsurgical strictures from all the different types of operations that Dr. Taylor has mentioned.

I would like to call your attention to a surgical procedure that is now being done at Presbyterian Hospital in New York City by Dr. David Habif. The operation is performed on patients who do not respond to conservative therapy.

(Slide) This patient has a hiatal hernia of the short esophagus type with ulceration stricture, and repeated hemorrhages.

(Slide) Dr. Habif, in making a repair of the hernia, used a section of jejunum and anastomosed it to the lower esophagus and also the upper portion of the stomach. He has done this in six cases and in each instance there has been no reflux and the anastomosis has worked very well.

In closing I would like to compliment Dr. Taylor on a most complete paper, one that I have found very instructive.

THE MECHANISM OF CLOSURE OF THE HUMAN LARYNX

BERNARD RAYMOND FINK, M.D.
NEW YORK, NEW YORK
BY INVITATION

AMONG the earliest observations on the mechanism of laryngeal closure in man are those recorded by Czermak one hundred years ago.[5] The newly introduced laryngeal mirror enabled him to show that closure of the larynx is a complex movement involving several events in a definite sequence. According to his observations, the arytenoid cartilages first make contact in the midline; next the false cords meet each other and, at the same time, approach the vocal cords; the ventricles thus become obliterated. Finally the epiglottic tubercle is lowered and presses against the closed glottis, completing the seal.

The appearance of the larynx as seen by mirror laryngoscopy led later observers to the development of the sphincter theory of laryngeal closure.[17] According to this theory, closure is produced by two superimposed layers of sphincters consisting of intrinsic muscles of the larynx: the aryepiglotticus above and the thyroarytenoideus and arytenoideus below. Some authors suggested that sphincteric contraction of the muscles was supplemented by a valvular effect.[4,12,18] They thought of the cords as cusps passively preventing the passage of air when in apposition. This idea gained some support from experiments by Brunton and Cash on cadavers,[4] but a roentgenographic study by Lindsay[11] clearly demonstrated that in the living body both the true and the false cords assume a shape which renders them incapable of acting as an outlet-closing valve. Lindsay's findings were fully confirmed by Ardran, Kemp and Manen.[1] Lindsay drew the conclusion that closure of the larynx must be by muscular action alone. More recently, Pressman placed renewed stress on the sphincteric role of the aryepiglottic muscle.[14] He compared its action to a purse-string closing the laryngeal orifice from side to side, with an anterior dehiscence filled in by the epiglottic tubercle and a posterior dehiscence closed by forward tilting of the arytenoid cartilages.

The concept of sphincteric action, ably reviewed in a recent article by Pressman and Kelemen,[15] does not explain all the known facts relating to laryngeal closure. It is not easy for the present author to accept the theory that the small muscles inside the larynx, unaided, are strong enough to resist the high intrathoracic pressure which develops when a severe cough or straining effort is made, or to prevent the insertion of an endotracheal tube by an anesthesiologist during laryngospasm. Furthermore, it is surprising that even when these intrinsic muscles are paralyzed, the larynx is still capable of closure. This has been demonstrated roentgenographically in a study by Ardran, Kemp and Marland[2] and is attested clinically by the fact that patients with bilateral recurrent laryngeal nerve paralysis nevertheless develop paroxysms of coughing when they attempt to swallow liquids. Such coughing involves a series of closures of the larynx, an effect which obviously cannot be ascribed to the par-

From the Anesthesiology Service, The Presbyterian Hospital in the City of New York and Columbia University, College of Physicians and Surgeons.

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alyzed intrinsic muscles. These considerations suggest that additional muscles are involved in the act of laryngeal closure and that sphincteric contraction of the intrinsic muscles is, at most, only one component of the mechanism. The present investigation was undertaken to explore this idea.

METHODS

External digital palpation was used to detect gross movements of the hyoid bone and of the thyroid and cricoid cartilages. This method was employed in order to avoid the distortions inevitably caused by introducing an instrument into the pharynx. Photographic records of the movements were obtained by means of roentgenography.

Roentgen studies were made on four healthy men. Lateral roentgenograms and anteroposterior laminograms were taken under the following conditions: end of normal expiration, sustained Valsalva maneuver (forced expiration with glottis closed), and phonation of "ah" at a pitch of 256 cps. The subject obtained the pitch from an audiometer earphone. Each lateral or anteroposterior series was made under constant conditions of exposure and position. Representative techniques were for lateral views: 400 ma., 72 kv., 1/10 second, tube-film distance 72 inches, centered over notch of thyroid cartilage; for laminograms: 50 ma., 52 kv., 3 seconds, tube-film distance 36 inches, plane 2.5 cm. posterior to notch of thyroid cartilage.

Direct laryngoscopy was used on six patients during general anesthesia to study the distribution of cough-provoking mucosa. The tests were made at the conclusion of operations for which anesthesia had been maintained with thiopental sodium, nitrous oxide and oxygen. Areas of mucosa were stimulated by contact with a blunt probe and the ensuing reaction was noted.

NOTE ON ANATOMICAL NOMENCLATURE

In the report which follows, frequent reference will have to be made to the portion of the epiglottic cartilage forming the anterior wall of the larynx. This portion extends from the attachment of the hyoepiglottic ligament above to the thyroepiglottic ligament below (fig. 3). Its posterior surface bears a midline prominence called the epiglottic tubercle and laterally receives the attachment of the aryepiglottic folds and the lamina quadrangularis. Its anterior surface gives attachment to the pre-epiglottic body. A descriptive term is desirable to facilitate reference to the intralaryngeal portion of the epiglottic cartilage, thus defined. The term "paraglottis" appears to be justified both by the position and by the function of this structure, and it will accordingly be used through the remainder of this paper. "Epiglottis" refers to the upper part of the epiglottic cartilage, i.e., the part lying within the pharynx.

OBSERVATIONS

1. *External Palpation*

The upward movement of the larynx which occurs on swallowing is readily palpable and can be detected by a fingertip placed in the notch of the thyroid cartilage below the hyoid bone. This movement has been regarded as bringing the larynx under the shelter of the tongue, out of the way of a descending bolus.[3]

Palpation shows that ascent of the larynx also accompanies coughing, straining and laryngospasm. In every case the upward movement is accompanied by cessation of air flow through the larynx, indicating that the larynx has closed.

A prolonged closure can be maintained voluntarily by straining, e.g., in a Valsalva maneuver, and as long as this

continues the thyroid cartilage can be felt to remain up against the hyoid bone. When the effort ceases, the thyroid descends to its resting position and air flow recommences, indicating that the larynx has reopened.

These observations suggest that upward movement of the larynx is a constant accompaniment of laryngeal closure and may be a necessary part of the closing mechanism.

2. *Roentgenograms*

Comparison of lateral roentgenograms of the larynx at rest and during a Valsalva maneuver (fig. 1) shows that in the latter the thyroid cartilage and entire larynx have moved upward relative to the hyoid bone. The distance between the epiglottis and the hyoid bone is increased. At the same time the paraglottis (laryngeal portion of the epiglottic cartilage) assumes a curved contour and bulges backward, coming into contact with the false cords as they sweep back towards the cuneiform and arytenoid cartilages. The upper surfaces of these structures form a continuous curve closely applied to the posterior surface of the paraglottis.

The paraglottic bulge is well seen during the upward movement of the larynx which accompanies phonation of certain vowels.[10] When "ah" is sounded (fig. 1, C), the paraglottis bulges backward just as in the Valsalva maneuver, but the upper orifice of the larynx remains open because the false cords are

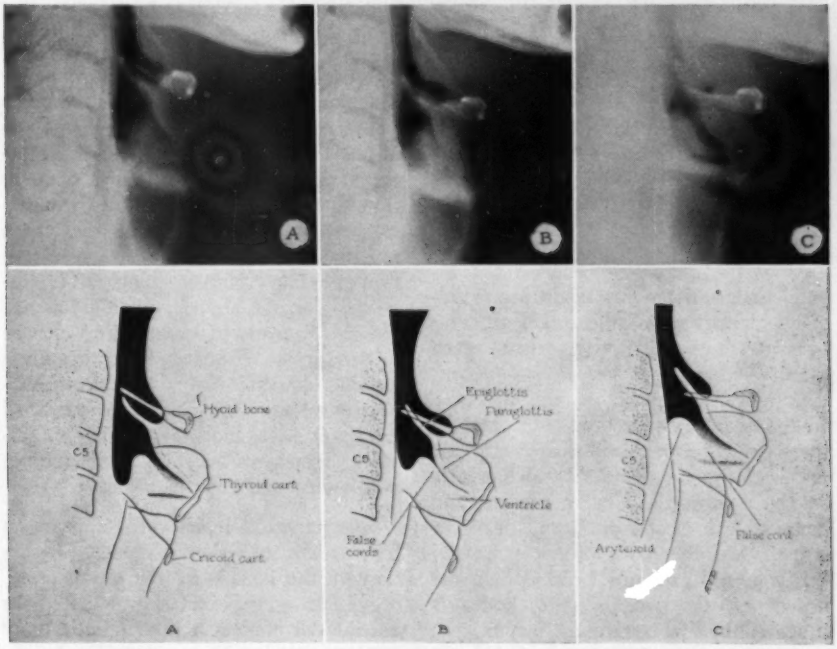

FIG. 1—Lateral roentgenograms of the larynx: (A) at end of quiet expiration; (B) during Valsalva maneuver, and (C) during phonation of "ah." Reduction of the distance between the thyroid cartilage and hyoid bone compresses the preepiglottic body and causes the paraglottis to bulge. During closure of the larynx the false cords are in contact with the bulge, but during phonation the false cords are pulled away from the paraglottis by the cricothyroid mechanism.

drawn backward by the arytenocricoid tilt incident to tensing the vocal cords.

Anteroposterior laminograms show that elevation of the larynx causes the upper horns of the thyroid cartilage to bend inward under the hyoid bone (fig. 2).

3. *Direct Laryngoscopy*

When observed through a MacIntosh laryngoscope during light general anesthesia, stimulation of pharyngeal mucosa and of the piriform fossa did not produce any reaction. The anterior and posterior surfaces of the epiglottic cartilage were also insensitive except at the lateral margins of the paraglottis. Contact of the probe with the upper edge of the aryepiglottic folds produced an immediate transient closure of the false cords. If the stimulus persisted, the false cords remained closed and the mucosa of the aryepiglottic folds was seen to roll inward, obscuring the cuneiform and corniculate tubercles and producing the puckered appearance typical of laryngospasm. Sometimes several coughs preceded the spasm.

DISCUSSION

Elevation of the larynx during a Valsalva maneuver has the effect of compressing the preepiglottic body between the thyroid cartilage and the hyoid bone. The preepiglottic body (fig. 3) is a wedge of fatty tissue limited in front by the thyrohyoid membrane, above by the hyoepiglottic ligament, and posteriorly by the paraglottis. The membrane and ligament are elastic and can shrink or stretch, but the paraglottis consists of cartilage and can only bend. When the tissue of the preepiglottic body is squeezed by the ascending larynx, the hyoid bone is pushed forward and the paraglottis is forced to bend and bulge backward. The false cords are attached to the thyroid cartilage immediately below the paraglottis. When the thyroid cartilage moves upward, the false cords must also rise and approach the paraglottis. The false cords and their posterior continuation, the cuneiform cartilages, are thus carried into contact with the paraglottic bulge, and closure of the larynx is completed. It is interesting to note that the original observations of Czermak[5] are entirely consistent with this concept.

The above mechanism may be compared to a ball valve. The ball is formed by the preepiglottic body, the valve seating by the false cords. Elevation of the larynx simultaneously makes a ball of the preepiglottic body and presses the valve seating, i.e., the false cords, against it. The stronger the elevation, the tighter the closure. The mechanism operates equally well whether the larynx is pulled up or the hyoid down.

Muscles which draw the thyroid cartilage and hyoid bone toward each other are required to set the ball valve in operation. The thyrohyoid muscles have attachments consistent with such a function, and Best and Taylor[3] in their discussion of swallowing state that these muscles are the ones which cause elevation of the larynx. Accordingly, it is suggested that the thyrohyoid muscles are the chief means of maintaining closure of the larynx. It is suggested that these muscles activate the ball valve mechanism whenever the larynx ascends toward the hyoid bone, not only during a Valsalva maneuver but also in coughing, swallowing and laryngospasm.

The paraglottic ball valve appears to be peculiar to higher primates. Dissection of the larynx of the chimpanzee, orangutan and gibbon shows that these animals all possess a preepiglottic body and paraglottis. On the other hand, cercocebus and macacus monkeys, and the cat, dog and rabbit are entirely lacking in such structures. Observation of the

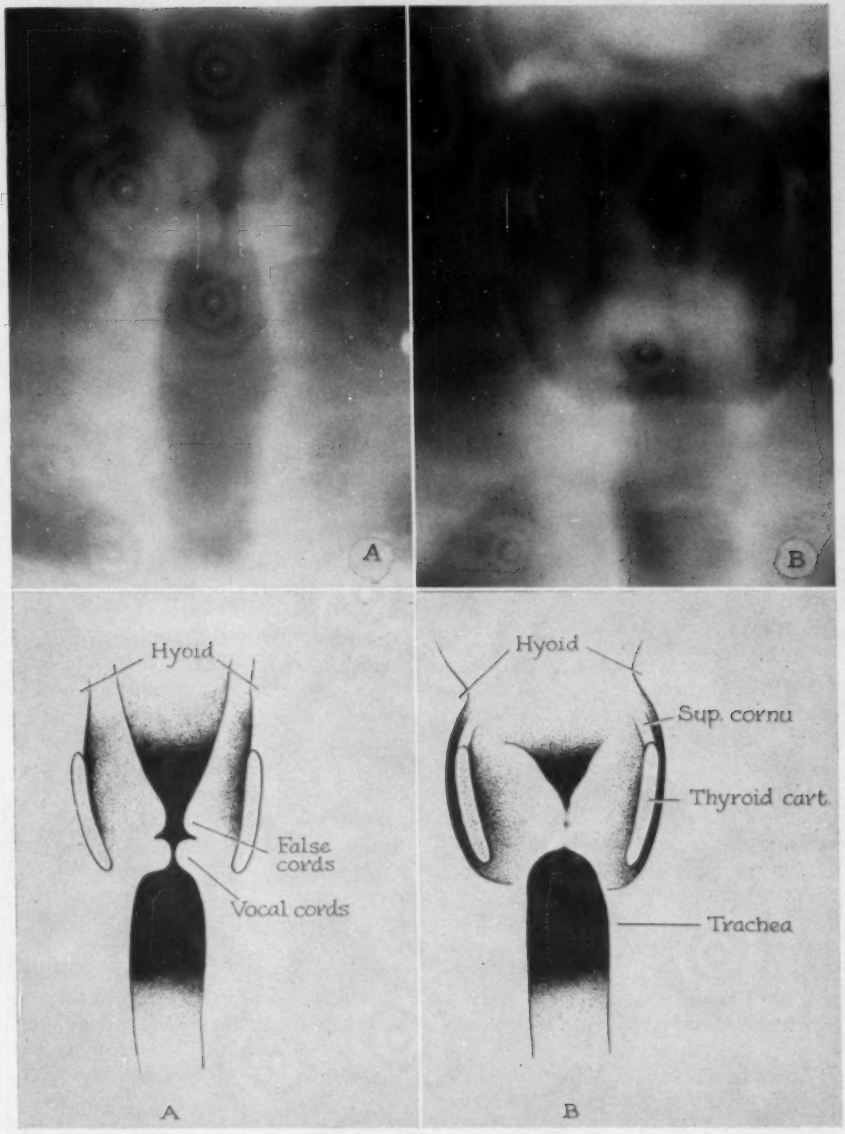

FIG. 2—Anteroposterior laminogram of the larynx at rest (A) and during a Valsalva maneuver (B). The upper horns of the thyroid cartilage bend inward under the cornu major of the hyoid bone. The false and vocal cords are in contact in the midline.

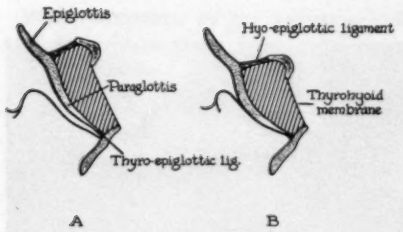

FIG. 3—Sagittal section through the preepiglottic body (diagrammatic): (A) larynx open, (B) larynx closed. During closure the larynx approaches the hyoid bone. The thyrohyoid membrane is shortened and the hyoepiglottic ligament stretched. The paraglottis (intralaryngeal portion of the epiglottic cartilage) cannot change in length and therefore bends.

cat, dog, rabbit and macacus monkey through a laryngoscope during light pentobarbital anesthesia shows that spasmodic closure of the larynx presents different appearances in each of these species, and all differ considerably from the appearances seen in man. Generalizations on laryngeal mechanisms including those of man have in the past been made from observations on widely different species, but in the light of the foregoing, such generalizations must be viewed with caution.

One of the consequences of the ball valve mechanism is that actual contact between the false cords cannot be regarded as indispensable for laryngeal closure. The upper orifice of the larynx will be closed even while the false cords diverge if the paraglottis is in contact with their upper surface. Clinical evidence for this is seen in patients with bilateral recurrent laryngeal nerve paralysis. Such patients can still close the larynx and produce a violent cough in spite of paralyzed adductors, because the thyrohyoid muscles are unaffected and can still elevate the larynx. This movement not only brings the paraglottic ball valve into operation but also causes the upper horns of the thyroid cartilage to converge (fig. 2) and indirectly brings the soft tissues inside the larynx closer together. Furthermore, as the false cords move upward they become flattened against the paraglottis, with the result that their free edges are driven toward each other.

CASE REPORT

Case 1—A woman, aged 35, was unable to phonate after undergoing total thyroidectomy. Mirror laryngoscopy showed the vocal cords immobile in a partly divergent position. Swallowing of water provoked violent coughing. Semisolid food could be swallowed without coughing. Figure 4 shows that performance of a Valsalva maneuver caused marked narrowing of the larynx in spite of bilateral recurrent nerve paralysis.

The present studies have not produced any evidence that the aryepiglottic muscles contribute to closing the larynx, whether by sphincteric action or otherwise. On the contrary, there are indications that the true role of these muscles is to open the upper orifice of the larynx during phonation. Goeppert[9] states that the aryepiglottic muscle is not present in any species other than man. The present author's dissections of the larynx of the orangutan, gibbon and chimpanzee, as well as of the dog and cat, revealed no trace of such fibers. It appears that in lower species, closure of the larynx is achieved without the aid of an aryepiglotticus muscle. The presence of this muscle exclusively in the larynx of man suggests that it is associated with a function peculiar to the human species, namely that of speech. High-speed motion pictures of phonation as seen through a laryngeal mirror[7] demonstrate that at the onset of vocal cord adduction the lateral walls of the vestibule become smoother and higher; the aryepiglottic folds become taut and elevated, with a sharp upper edge, as if supported by an underlying brace (fig. 5, A); the cavity of the larynx appears deeper and its entrance enlarged. It is suggested that these appearances are produced by contraction of the subjacent aryepiglotticus muscle and that this muscle makes its

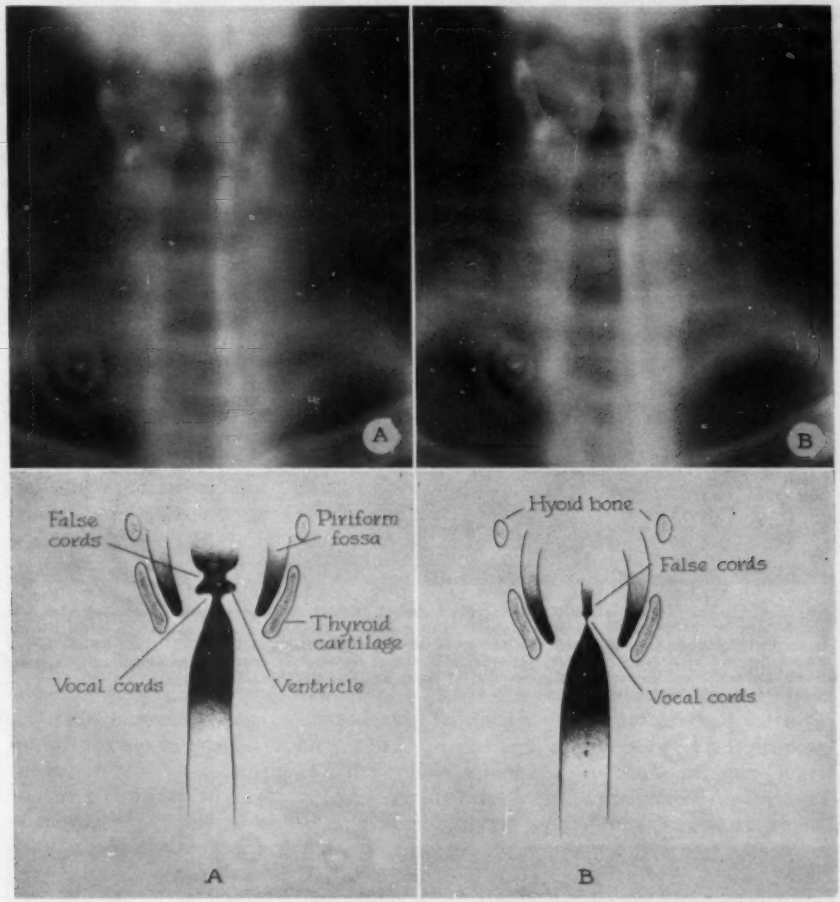

FIG. 4—Anteroposterior laminograms of the larynx in a patient with bilateral recurrent nerve paralysis (case 1); (A) at rest, (B) during a Valsalva maneuver. In (B) approximation of the cords has occurred in spite of paralyzed adductors. Vertical shortening of the thyrohyoid interval is unaffected. A nasogastric feed tube lies in the esophagus.

appearance in man not as a sphincter but, on the contrary, in order to enlarge the vestibule and thereby regulate the resonance of the larynx during the production of sound.

Forward tilting of the arytenoid cartilages has been suggested as contributing to closure of the laryngeal entrance.[13] However, such a tilt is not possible when the arytenoid cartilages are in contact, due to the shape and plane of the cricoarytenoid joints, as was indeed indicated by Fabricius[6] in his classic treatise on the voice.

Part of the actual mechanism that protects the larynx during swallowing has been beautifully demonstrated in a cinefluoroscopic study by Ramsey, Watson,

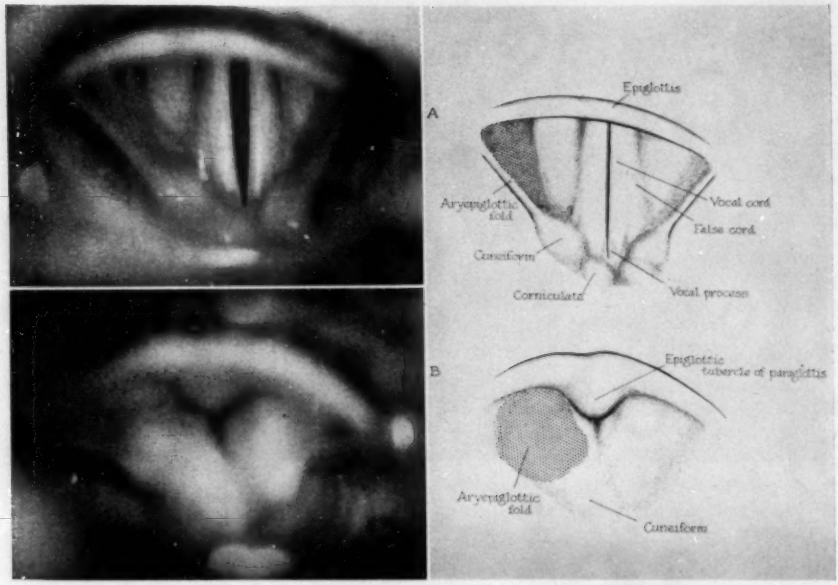

FIG. 5—(A) The larynx during phonation, photographed through a laryngeal mirror. During phonation the entrance of the larynx is sharply triangular. The mucosa of the aryepiglottic folds seems lifted upward by an underlying support, suggested contraction of the aryepiglottic muscles. (B) Entrance of the larynx toward the end of a cough. The aryepiglottic folds appear low and in contact with the paraglottis, as if drawn downward and forward in the direction of the isthmus of the thyroid cartilage. (Courtesy of Bell Telephone Company.)

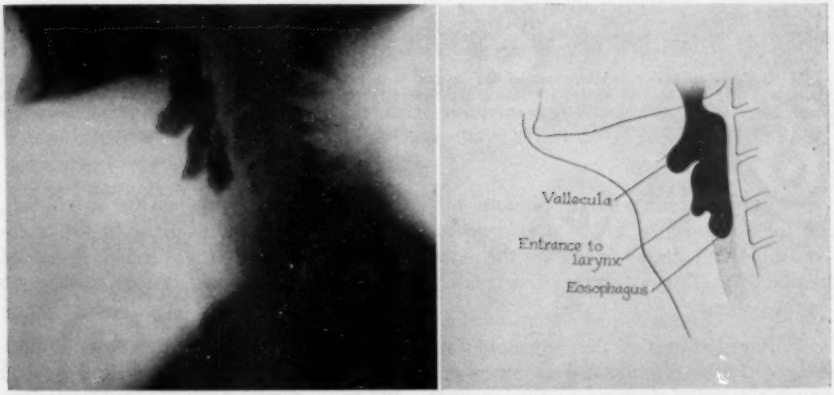

FIG. 6—The laryngeal region during the swallowing of a liquid bolus. Opaque liquid in the entrance of the larynx does not elicit a cough. (Courtesy of Department of Roentgenology, University of Rochester.)

Gramiak and Weinberg[16] at the University of Rochester. Their motion pictures show that the epiglottis (pharyngeal portion of the epiglottic cartilage) folds down over the larynx, but not always with the first swallow. When liquids are drunk, several gulps pass the larynx and appear to penetrate its entrance before the epiglottis folds over (fig. 6). With pasty food, the very first bolus pushes the epiglottis down ahead of it so that protection of the laryngeal entrance is present from the start.

It is necessary to explain how liquid can be present in the entrance of the larynx without provoking a cough. Stimulation experiments in the human larynx showed that sensitive mucosa capable of arousing a reflex closure begins right at the free edge of the aryepiglottic folds. Brief stimulation elicited a transient adduction of the false cords. When stimulation was more prolonged, the false cords met and appeared to rise toward the observer; finally the mucosa of the aryepiglottic folds became invaginated and produced the appearance typical of the larynx in spasm. A puckered funnel of mucosa was all that remained visible from above. In the Rochester motion picture of swallowing (fig. 6), swallowed liquid fills a similar funnel-like space in the entrance of the larynx without causing a cough. This suggests that the funnel is lined by insensitive mucosa, a result that could be produced by the same inversion of the aryepiglottic folds as seen in laryngeal spasm.

A comparable invagination seems to occur during coughing, although this movement is difficult to analyze because of its rapidity. Fortunately, the high speed motion picture of phonation made by the Bell Telephone Company[7] contributes valuable evidence on this question. It contains a sequence showing reopening of the larynx at the end of a cough. A frame from this sequence is reproduced in figure 5, B. The appearance is suggestive of partially invaginated aryepiglottic folds; these appear to be drawn forward and down in the direction of the pedicle of the epiglottic cartilage.

It seems, then, that sensitive mucosa at the entrance to the larynx is normally invaginated during closure, presumably to remove it from contact with swallowed food, so avoiding a reflex cough. The muscle producing this inversion is probably the thyroepiglotticus, attached below to the isthmus of the thyroid cartilage and inserted above into the lamina quadrangularis and the aryepiglottic fold. This mechanism is particularly important in the first phase of drinking, when it serves to protect the larynx before the epiglottis has become turned down over the top of the larynx. The mechanism will, of course, be inoperative when the thyroepiglottic muscles are paralyzed, as in bilateral recurrent laryngeal nerve injuries. In such circumstances no inversion of the aryepiglottic folds can occur although closure of the larynx by the paraglottic ball valve remains entirely effective. When drinking is attempted by these patients, liquid trickles over the uninverted aryepiglottic fold and immediately provokes a violent cough reflex.

The concepts emerging from this study lead to the view that closure of the human larynx is not primarily dependent on the intrinsic muscles. In man most of these muscles have become specialized for phonation, detracting from any sphincteric action they may still have in lower mammals. Indeed, two of these muscles, the aryepiglotticus and the vocalis muscle in the substance of the vocal cord, are not found at all in other animals, a fact which suggests that they are specially developed for human speech rather than for sphincteric action. The intrinsic muscles of the human larynx

may be regarded as constituting a muscular shutter with two layers and two functions. The lower layer is primarily concerned with phonation and is arranged to permit delicately controllable tension, thickness and length of the vocal cords. It consists of the arytenoideus muscle, the lateral and posterior cricoarytenoids, and the internal division of the thyroarytenoid. The cricothyroid muscle, which phylogenetically first appears simultaneously with the development of vocal cords in higher mammals (Goeppert), is also to be regarded as primarily a muscle of phonation. The upper layer is primarily concerned with closure and remains inactive during phonation. It is constituted by the external division of the thyroarytenoid muscle. Its function is the formation of a seating for the paraglottis: an approximation of the false cords preparatory to the operation of the preepiglottic ball valve. Thus the succession of movements observed by Czermak: adduction of the vocal cords, adduction of the false cords and formation of the paraglottic bulge, can be correlated with the phylogenetic development and the respective functions of each component. The evolutionary significance of these findings will be discussed elsewhere.[8]

SUMMARY

The mechanism of closure of the human larynx has been studied by external palpation, by roentgenography, and by direct laryngoscopy. The mechanism appears to be identical in swallowing, cough, straining maneuvers and laryngospasm. Sphincteric contraction of the intrinsic muscles is insufficient to explain all the features of these movements.

The present studies demonstrate the existence of a ball-valve mechanism of closure in the larynx of man. The ball is formed from the preepiglottic body and paraglottis (intralaryngeal portion of the epiglottic cartilage) and the valve seating from the upper surface of the false cords. This valve is operated by extrinsic muscles, including the thyrohyoid muscles, and is probably the most powerful part of the closing mechanism.

The concept is advanced that the true function of the aryepiglottic muscle is not sphincteric, but rather to enlarge the entrance of the larynx during phonation. There is suggestive evidence that the thyroepiglottic muscle is responsible for inverting the mucosa of the aryepiglottic folds during swallowing, in order to avoid initiation of a cough reflex.

ACKNOWLEDGMENTS

I gratefully acknowledge my indebtedness to the Department of Roentgenology of the University of Rochester and to the Bell Telephone Company for their interest in this work and for permission to reproduce figure 6 and figure 5, respectively.

The facilities of the Department of Otolaryngology in Columbia University, College of Physicians and Surgeons, were placed at my disposal by its Director, Dr. Edmund P. Fowler, Jr. To him, to Dr. DeGraaf Woodman, and to Dr. Vladimir Epanchin, whose skilled photography illustrates this article, I wish to express my sincere thanks.

Invaluable assistance was received from Dr. Juan Taveras and Dr. Russell Wigh of the Department of Radiology in Columbia University.

The case studies were made with the kind permission and encouragement of Dr. David Habif and Dr. Jules Waltner.

I wish to thank Dr. T. Donald Carter of the American Museum of Natural History for his courtesy in placing specimens and dissecting facilities at my disposal, and Mr. R. J. Demarest for the drawings.

To my chief, Dr. E. M. Papper, I am indebted for liberal and discerning advice.

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DISCUSSION

Joel J. Pressman, M.D., Los Angeles, California: Dr. Fink is to be commended for many reasons. First, he has taken it upon himself to step out of his field of anesthesiology and has dared to enter this den of lions with a subject as argumentative as this one is, one which has been debated fully for so many years. He is likewise to be commended upon his choice of his subject of basic physiology. The more we have of it, the more we will eventually learn about the action and the diseases of the larynx.

Dr. Fink has suggested widespread deviations from our long-established thinking that require a degree of proof that would be far-reaching, indeed. We have for so long accepted the principles of laryngeal sphincter action, and closure of the larynx dependent upon such action, due to intrinsic muscle action that for us suddenly to pick up our baggage and leave would be almost unthinkable without overwhelming proof that our previous reasoning along these lines has been in error.

I shall take up several of the points as Dr. Fink has cited them in his summary.

First of all, the concept of cough being dependent upon laryngeal closure is not entirely in keeping with the facts. A cough does not depend upon laryngeal closure. Cough can take place when the larynx is completely isolated from the upper respiratory tract as, for instance, when a tracheotomy tube is inserted. The action of the sphincters of the larynx is a quantitative thing, increasing the effectiveness of the cough, so that it is, roughly, 20 per cent less powerful when the sphincter mechanism is not intact; but cough can be produced and is, nevertheless, effective in animal experiments or in patients with diseases in which bilateral recurrent laryngeal nerve paralysis exists, or even when a tracheotomy tube has been inserted.

Dr. Fink states that the mechanism of closure of the human larynx is identical whether the closure is in swallowing, coughing, straining or laryngospasm. From the standpoint of action of the intrinsic muscles, this may be true. But Dr. Fink is speaking of the action of the extrinsic muscle, and in this instance it certainly is not true. For instance, in swallowing, the larynx is elevated well up under the tongue, so that the actions of the extrinsic muscles see their fullest play in this mechanism. On the other hand, in coughing or in straining, as in the Valsalva maneuver, the larynx does not necessarily rise up at all. In fact, we can close the laryngeal sphincter and lower the larynx at the same time.

One would gather from what I have just said that there is actually no direct relationship between the action of the extrinsic muscles and closure of these sphincters since the extrinsic muscles act in some of the processes indicated but certainly not in all.

That a valvular mechanism exists in which the so-called paraglottis or tubercle of the epiglottis plays a role, there can be no doubt, and this, as Dr. Fink has pointed out, has long been known. But there is actually nothing to indicate that this is a ball-valve mechanism. I think if this were true, then Dr. Fink should present evidence that the ball can be displaced by aerodynamic pressure from below, since this is a characteristic of ball valves. I have seen nothing in the presentation to indicate that this occurs; therefore, while it is agreed that a valve mechanism exists, one must look with skepticism upon the statement that the valvular closure is ball valve in nature.

There are several questions that need to be put to Dr. Fink.

First, if the sphincteric closure of the larynx is of extrinsic muscle origin, and is therefore paralyzed during radical neck dissection when the hypoglossus nerve is destroyed, why is it that closure of the larynx in the sphincter fashion remains as before? And why, conversely, after complete peripheral recurrent laryngeal nerve paralysis does the closure of the false cords sphincter ordinarily become lost despite the fact that the action of the extrinsic muscles remains intact? Occasionally, but only very occasionally, does the closure of the false cord sphincter remain intact following bilateral recurrent laryngeal nerve paralysis. But there is no reason why the action of the thyrohyoideus muscle should not remain intact. If it does, why do we find this sphincter closure to have been destroyed?

If one observes the laryngeal action as a patient forcibly squeezes a pillow being hugged by the arms against the chest, the larynx does not elevate itself; yet closure of the false cord sphincter occurs and is complete. I would be very much more likely to look with favor upon Dr. Fink's theory if he would change the concept from a false cord sphincter to the aryepiglottic sphincter, and I would like to demonstrate with slides the concept that we hold of the action of this false cord sphincter so that you can contrast it with the tenets held forth by Dr. Fink.

(Slide) This is a view of the larynx and of the aryepiglottic fold, of which he speaks. The latter extend outwards from the arytenoids which are placed posteriorly.

(Slide) This is the concept of the closure of these aryepiglottic folds and of the formation of a closed sphincter at this upper level. Here the aryepiglottis folds are approximated to the midline with the tubercle of the epiglottis coming into play and closing the anterior defect which would exist without it. This can be visualized easily enough by looking with a mirror or laryngoscope during gagging. It is hardly necessary to resort to the medium of roentgenograms to observe things that we can see by direct vision, or with a mirror or laryngoscope. The closing of this epiglottic fold during retching is too apparent to be denied.

This is a protective mechanism and takes place at this high level because if it were not so, and the protective mechanism were established at the level of the false vocal cords, it would be too far within the larynx to be effective, for when the false vocal cords ultimately opened, the foreign matter would fall into the trachea. Nature has, therefore, provided a closure high up at the level of the inlet of the larynx, which is represented not by the false cords but by the aryepiglottic fold.

The mechanism for protection of the lower respiratory tract varies greatly in different animals. For instance, some reptiles are able to protrude the larynx through the mouth to the outside world when they swallow. Others elevate it to well up under the tongue. Still others place it high up into the nose.

(Slide). This is a counterpart of the slide that Dr. Fink showed you, taken from the same source. I interpret "A" as being the free margin of the epiglottis, "B" as being the tubercles, "C" as being the arytenoid, and "D" as being the aryepiglottic fold extending to the midline. Ultimate conclusions depend upon what interpretation you put on the identity of this mass of tissue here. If these are the false cords, then the closure of the aryepiglottic fold in this picture has not taken place. But the fact that it has not taken place in this picture does not mean that it does not take place at any other time. It means only that in this picture, belonging to the Bell Telephone Company, and furthermore just in this frame of the picture, the closure of the aryepiglottic fold has not taken place.

(Slide) The closure of the true vocal cords is something else again. This is a series of closures of the true vocal cords, which close as a preliminary action preceding the closure of the false vocal cords above them. As you see here, the false vocal cords are sneaking in toward the midline, the beginning of the closure being anterior. Without the help of any epiglottic tubercle, they are closing themselves very completely. Here there is just a chink left, and in the succeeding stage of this sequence of photographs we see the complete

closure of the false vocal cords without the aryepiglottic fold entering into the picture at all.

I would like to show you in a motion picture film that closure of the larynx by the sphincteric action of the true and false vocal cords is not necessarily bound to any elevation of the larynx, or to closure the aryepiglottic fold, nor is it dependent upon the epiglottis, which is being held out of the way by the photographic laryngoscope.

[The motion picture was shown and consisted of photographs of the human larynx as the true and false cords closed in sphincteric fashion.]

I would like to see Dr. Fink demonstrate his principle during thoracic fixation rather than in an attempt to swallow. Swallowing is something peculiar unto itself and involves more than laryngeal closure. In the motion picture one sees sphincter closure with the true vocal cords closing at one level and the false vocal cords closing over the top of them. You can see the anterior limit, where the tubercle of the epiglottis is supposed to be. The false vocal cords close very effectively without it, the tubercle of the epiglottis being actually held out of the way so that you see it is not required for the closure. This is a very forceful, very effective closure, airtight, watertight, as tight as anything can possibly be. It is very forceful, indeed.

I think that probably if the thyrohyoid muscle plays any role in laryngeal sphincter closure, it must be not at this level but at the higher level of the aryepiglottic folds. Here we see the closure of the false vocal cord sphincter without it.

My objections do not mean that Dr. Fink is not correct. They mean only that in certain examples of closure of the larynx he is not correct. He may be absolutely right in the mechanism which he describes. The evidence for this could be forthcoming in several ways; for example, by severing the muscle intentionally when the larynx is to be removed and observing the subsequent action of the sphincter. But until such evidence is forthcoming, I think we should not entirely abandon our concepts which seem to have borne the test of time.

OSCAR V. BATSON, M.D., Philadelphia, Pa.: Before discussing the closure of the larynx, I state two criticisms. I do not like the term "paraglottis," since para means alongside and the glottis is the slit between the two vocal cords. As I see it, the lower part of the epiglottis is still above the glottis. I also object to anthropomorphic anatomy; that is, the anatomy that states that a particular structure develops to further some function. This line of reasoning, or perhaps it is only a method of statement, would lead to the conclusion that we have an external nose in order to support our eyeglasses.

The closure of the larynx is especially significant in man, since we use the upper extremity for lifting and pushing. I believe that we have two different kinds of closure of the larynx: (1) the closure which accompanies straining, as in lifting, and (2) the reflex closure of the larynx in spasm. The first type keeps air in the chest, the second prevents its entrance. If these two closure types were kept clearly in mind, perhaps some of the differences between Dr. Fink and Dr. Pressman would be clarified.

Not all branches of the superior laryngeal nerve need carry the stimuli for the spasmotic closure of the larynx. Lewenfisz [Rev. de laryng., 59:311 (March) 1938] showed that stimulation in the piriform sinus in dogs causes respiration to stop in the expiratory phase. This is true even with a tracheotomy tube in place. Too often we see interns use an aspirator tube during tonsillectomy as if it were a potato masher. Some of the difficulties encountered by the anesthetist could be due to stimulation of the superior laryngeal nerve by the rough use of the aspirator.

The concept of muscle contraction protruding the laryngeal fat body over the glottis has been illustrated by Von Lanz and Wachsmuth. It is not wholly clear how these authors arrived at this concept.

Dr. Fink has brought together a large series of clinic and radiographic observations, and he has organized them in support of this concept. He has interpreted them in the light of the anatomy of the region. Correlations like this in other areas would be helpful. It may well be that false cords in closing the glottis are actively aided by this corpus adiposum laryngis, which is pushed into position by the thyrohyoid muscles.

DR. FINK: I would like to express my thanks to Dr. Pressman and Dr. Batson for the way in which they have considered and discussed this presentation.

I would like to say to Dr. Pressman that we have made electromyographic studies of the larynx during these various movements, with no less than six concentric electrode needles simultaneously in place in order to explore the pattern of activity of the laryngeal muscles, and I think it can be said that the results, which are not complete yet, appear to confirm the thesis of the paper.

VOICE REHABILITATION
via
LARYNGEAL SURGERY AND SPEECH THERAPY

DEGRAAF WOODMAN, M.D.
and
SHULAMITH KASTEIN
BY INVITATION
NEW YORK, NEW YORK

WE are all aware of the strides that the speech therapist has made in the rehabilitation of those patients handicapped by the loss of part or all of their larynx. The use of surgery as an aid to voice rehabilitation, independent of the removal of laryngeal growths or problems secondary to various laryngeal paralyses, is relatively uncommon. I believe it to be a surgical field which offers opportunity for further development.

The case to be shown presented a not uncommon finding—a small web at the anterior commissure of the larynx. Such a web sometimes occurs secondary to an inflammatory process, or as the result of trauma during removal of polypoid growths from the vocal cords in the region of the anterior commissure.

CASE REPORT

Miss S., age 38, gave a history of having had croup as a child, which was so severe as to require a tracheotomy. The tracheotomy tube was left in place for eleven days, and the child remained hoarse for two years. During primary school days she was able to sing, although her voice was not good. In 1950 she developed a hoarseness which persisted for two years. She consulted a physician, who stated that she had a laryngeal polyp. He removed the polyp, but she remained aphonic for four months. This was followed by a laryngoscopy, with further attempts at removal of polypoid tissue resulting in only slight voice improvement. The report of the last biopsy was also laryngeal polyp. The voice remained hoarse.

This patient was first seen by me in the fall of 1952. The voice was whispered in quality, and there was a small web at the anterior commissure (fig. 1). This prevented satisfactory use of the true cords and accounted for the whispered type of voice.

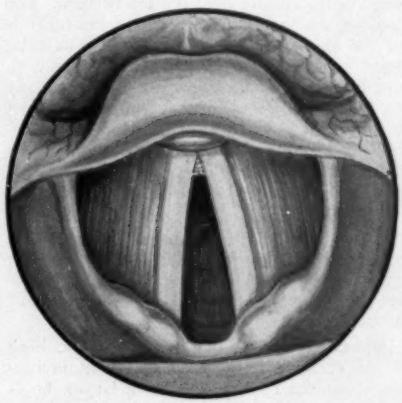

FIG. 1—Anterior commissure web.

Since there was no embarrassment in the airway, it was thought that the patient might improve with voice therapy, and her physician referred her to one of the speech disorder hospitals, where six months of therapy failed to result in any relief or improvement.

We then suggested trying to rid her of the web via a McNaught[1] keel procedure, which she agreed to. The keel was placed via a thyrotomy approach as described by McNaught and shown in figure 2. The following day, roentgenograms demonstrated the anterior-posterior and lateral views of the keel in posi-

Presented at the Sixtieth Annual Session of the American Academy of Ophthalmology and Otolaryngology, October 9-14, 1955, Chicago.

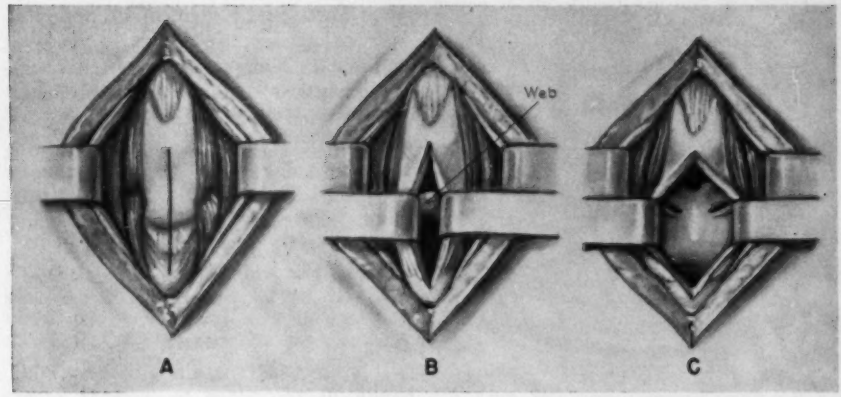

FIG. 2—McNaught's thyrotomy for placement of keel.

tion (fig. 3). The diagramatic sketch (fig. 4) shows the relationship of the keel to the laryngeal structures.

Eight weeks later the keel was removed by an external approach. Recordings of the voice one month following keel removal show little or no improvement. At this time an indirect view of the larynx showed the anterior commissure free of web (fig. 5). After two months of speech therapy, definite improvement was noted in the recordings. Recordings taken two years later demonstrate rather marked improvement in tone, quality and strength of voice.

The pattern of voice therapy given is outlined by Shulamith Kastein, Speech Pathologist at the Vanderbilt Clinic:

"In order to help this patient reduce strain and tension of the laryngeal muscles and to produce voice on a level approximating optimum pitch, the *chewing method*[2] was used as the therapy of choice; in her case, at a pitch lower than usual for her. In introducing the chewing method, the patient was asked to

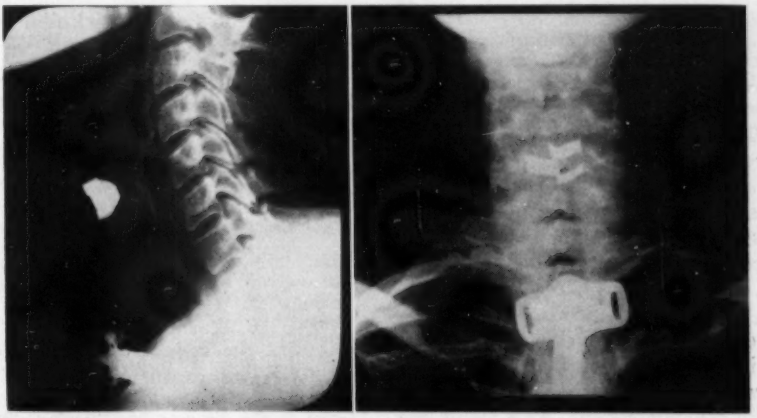

FIG. 3—Roentgenograms showing anteroposterior and lateral views of larynx one day after placement of keel.

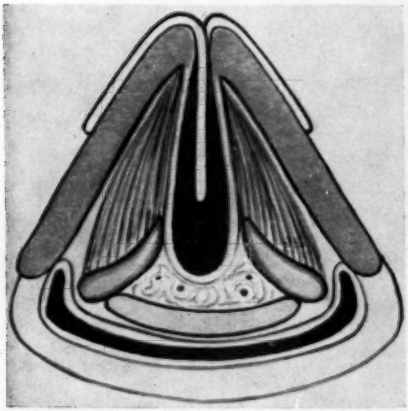

FIG. 4—Relationship of keel to laryngeal structures.

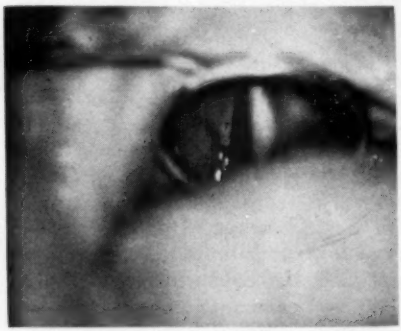

FIG. 5—Indirect photograph of larynx after removal of keel.

think of chewing food, but to chew with voice emission, that is loudly and without keeping the lips closed. The importance of actually chewing, rather than imitating chewing movements, was stressed. Loudly chewing numbers, the days of the week and single words followed. When this could be done, phrases and sentences were chewed aloud, and the patient was encouraged to read aloud, each word being chewed. The immediate goal was to help the patient chew English rather than to speak it for all communications. As a result, the voice became clearer and louder, the pitch lower and closer to the optimum appropriate for the patient's age, sex, and build. The patient reported spontaneously less strain in the larynx and less fatigue when speaking, as well as relief from pain and discomfort. To complete and round out the therapeutic program, diaphragmatic breathing was taught, as well as breath control to eliminate air waste. Jaw shaking with phonation was also added."

COMMENT

It is suggested that those patients with handicaps secondary to traumas from laryngeal biopsies or inflammations be examined carefully with the thought that removal of the web, even though small, may offer a means of permitting proper function of the true cords. When such surgery is combined with postoperative speech therapy, it may aid considerably in voice rehabilitation.

SUMMARY

A case report has been presented which demonstrates the value of combined surgery and speech therapy for the rehabilitation of voices handicapped by webbing at the anterior commissure.

A kodachrome sound-track film* was shown to demonstrate the technique described, with recordings of the voice preoperatively, postoperatively and following speech therapy. Views of the vocal cords before and after surgery were shown.

REFERENCES

1. McNaught, Robert C.: Surgical correction of anterior web of the larynx, Laryngoscope, 60:264 (March) 1950.
2. Weiss, D. A., and Beebe, H. H.: The Chewing Approach in Speech and Voice Therapy, Karger, 1952.

* Copies of this film may be obtained or rented through Sturgis-Grant Productions, Inc., 322 East 44th Street, New York 17.

DISCUSSION

NATHANIEL M. LEVIN, M.D., Miami, Florida: This presentation clearly shows what cooperation between a surgeon and a speech and voice therapist can do. Neither surgery alone nor voice therapy alone could accomplish what has been demonstrated in this instance. Laryngeal surgeons have been working more closely with voice therapists in organic and functional vocal problems, in some of our larger institutions and centers; now we are beginning to see this in private practice also. There is nothing new in such a procedure. We have been working together with audiologists for some years now, for the benefit of our patients. This cooperation is providing a type of service that neither one alone can give, and it is to be encouraged. Also, at each of our Academy meetings, a number of papers and courses on the pathology and therapy of diseases affecting speech and voice are being given. An increasing interest is being shown by our fellow members in these presentations.

All of us are seeing clinical conditions that are comparable to the case that Dr. Woodman demonstrated to us. We are very pleasantly surprised by the results obtained by a voice therapist in these cases. I am referring to certain vocal nodules, contact ulcers, and others. The lesion is removed once, twice, or repeatedly, only to recur. It is apparent now that further surgery without correcting the underlying misuse of the voice may result in scarring and further damage to the vocal cords. The patient does not like it. He judges the results of our laryngeal surgery by the type of voice he gets, and it is hard for him, as a layman, to understand what the difficulties are. He has been listening to a barrage of cancer propaganda, and he begins to ask the doctor, "Don't you think I have a cancer?" He is becoming a little uneasy, so that it becomes necessary for us to attempt voice rehabilitation a little further. In these cases, surgery alone is not enough. A number of laryngologists are doing speech therapy themselves and are becoming well known in this field. Others may not have the time or inclination to do so and refer the case to, or work with, a voice therapist. In treating the professional, it is very important to consider his special requirements and working conditions, as well as his emotional problems.

As an instance, I removed a contact granuloma (ulcer) from the larynx of a salesman, and he went back to work with a good voice, after a short period of voice rest. Two months later, his voice was just as bad as before. There was recurrence, with the development of another contact ulcer much larger than the first one. I explained the problem of vocal misuse to the patient and told him how effective voice therapy can be; I encouraged him to start working with a properly trained therapist. Within thirty days the large lesion had diminished considerably, and at the end of eight weeks the granuloma had completely disappeared.

Granulomas appearing on the vocal cords following endotracheal anesthesia, and which recur after removal, present a problem similar to that of contact ulcer. Further experience is required to determine what the proper therapy should be, whether surgical removal and/or voice therapy. After repeated biopsies indicate that the lesion is benign, vocal therapy will expedite the return of a more normal voice.

Vocal disturbances without actual paralysis are often seen by laryngologists and general surgeons following thyroidectomy. This is a mild paresis. In some cases, on mirror examination one arytenoid is seen to be more anteriorly placed than the other; thus the cord may be shorter or more flaccid, or one vocal cord is on a lower level than that of the opposite side. Only one or several branches, not the entire nerve, are involved, in accordance with the newer anatomical studies of the recurrent laryngeal nerve. Such post-thyroidectomy patients, if allowed to go on by themselves get into difficulties from a forced pattern of vocal abuse (hyperfunction). Occasionally such a patient will develop a cordal submucosal hemorrhage or polyp. These patients must have vocal retraining.

A logical question is, "Why do such patients get into vocal difficulties?" It seems that after a prolonged case of laryngitis or after laryngeal surgery, an individual may lose his kinesthetic sense. We monitor our speech and voice mainly by our hearing; but there is also a subjective feeling about it. This is especially true in singing. If a singer loses this monitor, he may wander off on the wrong path, vocally. An experienced voice therapist can show him the proper way.

As laryngologists, most of us have always been interested in speech and voice, but it is apparent now that more recently there has been a greater interest, due to the increasing number of patients who require our services. Because more people are cancer conscious, disturbances of voice bring them in. Also, the radio and television have been very effective in making people realize what a good voice is, and now they come in more readily for an opinion or treatment.

With only a few minutes remaining, I will not take time to discuss the surgical aspects of Dr. Woodman's case. I might say some-

thing about voice rest. Generally when a patient is discharged, he is placed on "voice rest." Sometimes we are not too specific with our orders, or the patient may make his own interpretation or may even fail to follow our instructions. He may be told to whisper. If done correctly, this is truly without voice. However, the patient actually may use a stage whisper, which is definitely not aphonic and is sometimes very forceful. Therefore it is better to order complete silence, rather than whispering, which may be done incorrectly or abused.

For how long should we put a patient on a voice rest regime? Only for the period that is required for the raw surface to heal, since that is the purpose of the voice rest. The average little benign lesion that you remove, if it has a small base, will result in a small raw surface, which takes only a few days to heal. If it is a sessile type of growth with a larger base, a little more time is required, perhaps two or three weeks. If you do a stripping of the cord, such as you do for polyposis or hyperkeratosis, you may have to give them a prolonged period of voice rest. These "stripping" cases are sometimes a little unsatisfactory to deal with. You know how much difficulty one may encounter, particularly if there is extensive involvement of one or both cords.

For professionals, the order of voice rest may do more psychological harm than the benefit to be derived vocally. Some of them are highly emotional people. They are going to worry; it may mean their careers. Before you sentence them to six weeks of silence, you have to consider it carefully. It is necessary to explain why it is going to take so long and what type of voice to anticipate after this period. Treating a patient with a functional vocal disorder for "laryngitis" is a waste of the patient's valuable time and may cause permanent vocal damage. A laryngeal mirror examination is not enough. The actual reason for the voice disturbance must be found. Is this a myasthenia laryngis? If the prognosis for voice is not good, the patient must be prepared emotionally for this.

In concluding, I want to say that Dr. Woodman should be commended for his efforts and the initiative shown in these special aspects of laryngeal surgery, aimed at improving the voice. His work has been outstanding in the open approach to arytenoidectomy for bilateral paralysis, corrective operations for laryngeal stenosis, and now this treatment of laryngeal web. Work of this kind adds another small but important segment to the changing field of otolaryngology.

FRANCIS E. LEJEUNE, M.D., New Orleans: Dr. Woodman has focussed attention today on a very interesting and difficult otolaryngologic problem. The results presented and achieved are excellent. The use of a tantalum splint, suggested by McNaught, has greatly simplified the correction of congenital webs, synechias and adhesions occurring between the vocal cords. We have had occasion to use this method in several cases of congenital webs, in cases that developed synechias following repeated removal of multiple papillomas, in injuries to the larynx, and in cases in which it was necessary to remove both vocal cords for existing malignancies. When a carcinoma of one vocal cord with extension across the anterior commissure has been removed, webbing may develop postoperatively. The removal of both vocal cords will usually be followed by considerable reaction and extensive synechias and webbing. The use of the McNaught splint in these cases is most gratifying. We have found that teamwork facilitates the operative procedure: while one surgeon exposes the thyroid cartilage through a midline incision, the other one introduces the suspension laryngoscope, exposing the larynx to direct vision. The webbing is incised in the median line through the mouth and dissected free from the edge of the cords, using a straight-edge laryngeal knife. Following this and still working through the mouth, a no. 15 curved blade on a laryngeal knife handle is inserted through the thyroid cartilage at the level of the vocal cords. This knife point emerging through the cartilage indicates to the surgeon working in the neck the exact area where the incision must be made in the cartilage for the insertion of the tantalum splint. Meticulous care must be exercised to make the incision in the cartilage perfectly straight so that the splint will remain in the median line between the cords; it should also be small so that the splint will fit snugly into it. As soon as the splint is introduced into the incision, it is visualized perorally, grasped with forceps and placed in the proper position. It is important that the tantulum splint should not be too long, as too long a splint will produce trauma in the interarytenoid region. We have found it advantageous to suture the splint when it is in place. Dr. Woodman did not mention whether granulating tissue developed in the anterior portion of the larynx in these cases, and if so, how he handled such an event. Practically all our cases developed granulating tissue, and we have found that the use of meticorten is advantageous in such cases. No webs developed following removal of tissue for biopsies, and cases of marked bilateral polypoid degeneration of the vocal cords can

be successfully operated upon without resulting webs if the virginity of the anterior commissure is respected. We have had no reason to resort to speech therapy in these cases, as vocal improvement followed correction of the existing defect; however, as shown by Dr. Woodman, voice rehabilitation offers much to these patients.

DR. WOODMAN: I appreciate very much the discussions by Dr. Levin and Dr. LeJeune. It was not my aim in this paper to discuss the keel procedure as used for the eradication of growths or the removal of obstructions causing dyspnea; that we have done in several cases and had considerable success without complications of granulations. In this paper we wished to describe the keel procedure as it was applied to the removal of a small web that had handicapped the voice. That was the only difficulty this patient had. It was the kind of web that many of us see and would hesitate to touch for fear we might do more damage than good. I think we can see that in this particular case it turned out to the patient's advantage.

I was very much interested in hearing of Dr. LeJeune's technique. The first two keels which I did were done under the guidance of a cooperating surgeon using a laryngoscope, but for the last four I haven't resorted to that procedure. We seem to reach the midline without the need of always looking through the laryngoscope.

THE UNDERGRADUATE TEACHING OF OPHTHALMOLOGY

ALAN C. WOODS, M.D.
BALTIMORE, MARYLAND

I WAS delighted when Dr. Ruedemann asked me to open this discussion. The problem of the proper organization of an undergraduate course in ophthalmology has interested me intensely over the thirty-six years during which I have taught medical students. In this period I have organized and reorganized various courses of instruction, have written and rewritten countless lectures, and have endlessly quizzed students at examination for the main purpose of ascertaining how successful I had been in imparting information to them, how much had been absorbed, and how much had gone over their heads. These students were almost without exception highly intelligent men, interested and eager to learn. When I found them ignorant of what I had thought had been carefully and well explained, and analyzed the causes of their ignorance, I found it was almost invariably my fault. It was the old story of crowding too much into a lecture, giving it too fast, and presenting it in an uninteresting manner! I must freely confess that I do not yet know all the answers to the various problems of undergraduate pedagogy. I can, however, tell you what I have learned by experience, by small successes and by many failures.

In the beginning, let me start with the premise that forty years ago, as a general rule, the undergraduate training in ophthalmology was a pretty disorganized, happy-go-lucky affair. Any exceptions to this rule were due to the individual brilliance and magnetic personalities of a few individuals genuinely interested in teaching. The conventional pattern then in vogue, and unfortunately still followed in some schools, was an uninspired series of lectures on the physiology of the eye and on methods of examination; much dreary instruction in refraction, muscle anomalies and strabismus; and routine discussions of diseases of the lids, lacrimal apparatus, the conjunctiva, the cornea, the sclera, the uveal tract, the retina and the optic nerve. The pathogenesis of these diseases was the concern of the bacteriologist, the pathologist and the internist—not of the ophthalmologist. The fault in this sort of teaching lay not in the instructor but in the tendency to regard the eye as an isolated organ, with its own private set of specific diseases; and the futile effort of the teacher to cover, in some manner, the whole subject of ophthalmology as presented in the small popular textbooks of that day. The clinical instruction in the out-patient departments was almost equally poor. The attending ophthalmologists were all busy practitioners, and their chief anxiety appeared to be to get the clinic finished up and get back to their practices or their amusements. There was not much time for the instruction of the student. He hung around, picked up any pearls of wisdom that fell his way, and then went home!

From The Wilmer Ophthalmological Institute of the Johns Hopkins Hospital and University.
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In planning a modern course in ophthalmology for undergraduate medical students, there are a few cardinal points which must be constantly kept in mind. The medical student usually begins the study of ophthalmology in the third year, when he is suddenly deluged with a plethora of clinical instruction in physical diagnosis, medicine, surgery, psychiatry, and the various medical and surgical specialties. No matter how brilliant the individual student may be, there is a definite limit to the amount of information he can absorb. The competition for his attention is intense. Each instructor, in all the various subjects, is on his mettle to capture the interest and the imagination of the student. The successful teacher of ophthalmology is therefore the one who can stimulate and hold the interest of his pupil in his specialty. If he is more successful in this than are his colleagues in the sister specialties, there is always the excellent chance that he may guide the best brains of the class into ophthalmology! Therefore, the first point to be remembered in formulating our undergraduate instruction is that the student should be fed no more than he can readily assimilate, and that this material should be served up to him in the most appetizing and appealing manner. The second cardinal point to be remembered is that barely one per cent of the class will ultimately become ophthalmologists and that an undergraduate course is not the place to teach the special disciplines of a specialty. The medical student should therefore receive instruction only in those phases of ophthalmology which will be of actual use to him in the later practice of his profession as an internist, a surgeon, or a specialist in some field other than ophthalmology.

In designing the course in undergraduate ophthalmology, there are, therefore, several pertinent questions to be answered. These are: What are the particular phases of ophthalmology which should be covered in this course? In what manner should instruction in these subjects be imparted to the student? In what sequence should it be presented? On these points there will be a wide variance of opinion. Again, I can give you only my own views.

The phases of ophthalmology which I believe will be of greatest value to the average physician in his practice, and which I believe should be the major subjects for undergraduate instruction, can be grouped under five general headings:

A. The reaction of the eye to acute exogenous infection and insult

B. The common intrinsic ocular diseases: cataract, glaucoma, and the degenerations

C. The reaction of the eye to metabolic disorders and systemic diseases

D. The reaction of the eye to systemic infections and hypersensitive disease

E. Neuro-ophthalmology

My reasons for this selection may be summarized as follows:

A. Every physician may be confronted at any time with the problem of an acutely inflamed or injured eye. An exact differential diagnosis is unnecessary; it is enough that the physician differentiate trivial inflammations and injuries from the serious ones, that he be able to prescribe first aid, and that he be wise enough to refer the patient to an ophthalmologist when the injury or infection is serious. To this end there should be instruction in the common external diseases and minor injuries, and in the differentiation of these from the deeper, serious inflammations and injuries.

B. Whatever may be the specialty of the physician, if he practices clinical medicine, a large number of his patients will develop cataracts, glaucoma, and the degenerative ocular diseases. Every

practicing physician should have a superficial knowledge of these, be on the lookout for them in his patients, and be able to discuss the general problems they entail.

C. If a physician is to treat the metabolic diseases—thyrotoxicosis, diabetes, the blood dyscrasias, etc., he must have some knowledge of their ocular complications. This is so axiomatic that it does not require discussion.

D. The reaction of the eye to systemic infections and hypersensitive disease embraces the entire question of endogenous uveitis, and all the ocular manifestations of both granulomatous and nongranulomatous systemic disease.

E. The ocular complications of the more common neurological diseases and of intracranial tumors should be the subjects of a short series of lectures. These lectures can well be supplemented by a series of elective clinics in ophthalmic neurology. These clinics are usually so spectacular that they are immensely popular, and they can be given outside the regular course with considerable assurance that they will be well attended.

In presenting the subjects of the reaction of the eye to systemic disease, metabolic disorders, and infection, the fact that the medical student is studying to be a doctor and is not being trained as an ophthalmologist should always be remembered. Therefore, the subject matter should be presented against the background of the systemic disease, and not as a specific disease of ocular tissue. For example, the usual interstitial keratitis of children should be demonstrated as the most frequent and important lesion of congenital syphilis, and not from the viewpoint of the ophthalmologist, that congenital syphilis is the most important cause of interstitial keratitis. Similarly, the retinopathies of diabetes, nephritis, arteriosclerosis, and the blood dyscrasias, should be presented as part of the complications of these diseases, their position in the disease complex stressed, their peculiarities emphasized, and the diagnostic importance of their peculiarities pointed out. This approach stimulates the student's interest, makes him regard ophthalmology as an integral part of his medical education, and teaches him to use his knowledge of ophthalmology as a diagnostic aid. Moreover, it prompts him to bring his patients with fundus lesions over to the ophthalmology department for discussion of the ophthalmological problems involved. And not infrequently, this aroused interest and informal personal discussions with a student result in recruiting good men for our specialty!

Just as certain phases of ophthalmology should be stressed, other subjects should be avoided or only lightly touched upon. Chief of these are refraction, muscle anomalies, and ophthalmic surgery. Instruction in errors of refraction can profitably be limited to simple definitions and explanations of hyperopia, myopia, astigmatism, accommodation and presbyopia. All the undergraduate student needs to know about anomalies of the ocular muscles is the difference between paralytic and nonparalytic squint, and the relation of accommodation and hyperopia to the common internal strabismus of children. All of this material can readily be covered in the preliminary lecture on physiology, and thereafter dismissed for the balance of the course. If discussed at greater length, one can be assured that the student will lose interest and will promptly forget all that he is told. Much the same applies to ophthalmic surgery. Here I believe instruction should be limited to a simple explanation and motion pictures of cataract and glaucoma operations, which should be a part of the lectures on these subjects. If the student becomes intrigued by these motion pictures, he will come to the operating room of his

own accord, watch various operations and ask questions. One such voluntary convert is worth a hundred unwilling victims, down whose gagging throats one crams an unwanted and indigestible meal!

Having reached a decision about the general subjects to be covered in the undergraduate course, the teacher must now decide how this material is to be presented to the student—through didactic lectures, through personal clinical instruction with the actual patient as the text, or through a combination of the two methods? The answer to this question depends somewhat on the amount of time available. The number of hours assigned to the required courses in ophthalmology varies within a wide range in different medical schools. The minimum is about twenty-six hours, and the maximum is occasionally over a hundred hours. The average is about forty-eight hours. Elective courses of almost any extent desired can usually be offered to supplement the required course.

What now are the advantages and disadvantages of didactic and clinical teaching? Didactic instruction, through planned and organized lectures, allows the available time to be used to the maximum advantage, permits the extensive use of auditory and visual aids, and avoids repetition. The chosen material is covered as desired, and each student receives the same instruction. Didactic teaching has the great disadvantages that the student is divorced from the patient and that the teacher loses personal contact with the student. It requires a most gifted teacher and artfully used visual aids to keep straight didactic instruction from becoming monotonous. And if it becomes monotonous, it becomes almost worthless.

The personal instruction of small groups of students, either at the bedside or with the ambulant patient present to serve as a text for the presentation of the subject, is probably the very best type of clinical teaching. It has the great advantage that the student can examine the patient, can see the actual lesions of the disease, can ask questions, and with his instructor can explore all the ramifications of the disease entity under discussion. Such instruction also has the invaluable asset to the student of close contact with both the patient and the instructor. I believe this form of teaching is the *sine qua non* for the graduate training of an ophthalmologist, and I cannot overstress its value in teaching medical students. But it has great disadvantages if it is the only method used to teach undergraduates. Primarily, it is difficult, or even impossible, to regulate the flow of the clinical material to the end that the patient with the proper disease is available at the right time for demonstration. Thus if we are dependent solely on clinical material for the subject matter of our teaching, our course in ophthalmology is liable to wander off into all sorts of strange byways, and students in the different quarters are likely to get quite different instruction. An orderly course becomes impossible, and our teaching efforts wind up in confusion. Further, since the great value of this type of teaching is the contact of patient, student and teacher, and the opportunity it affords the student to examine the patient, it is obviously applicable only to small groups. It is not applicable to a large class or when the time available for instruction is limited.

It is apparent that both didactic lectures and clinical teaching to small groups have their advantages and their disadvantages. Some compromise between them is necessary. A reasonably satisfactory arrangement is to divide the total allotted time equally between didactic instruction and clinical teaching. Thus, if there are forty-eight hours available for the required undergraduate

courses in ophthalmology, twenty-four of them can be allocated to didactic lectures, and twenty-four to group clinical teaching. For several years I attempted to integrate a didactic lecture and clinical teaching into one organized session. To that end there was first a formal lecture with many slides illustrating the lesions of the disease under discussion. At the conclusion of the lecture, a number of patients showing the symptomatology just discussed were assembled, an individual instructor was assigned to each two or three of these patients, the class of seventy-five was divided into small groups, which were supposed to rotate through the demonstrators and thus have opportunity to see and discuss the actual lesions. This idea seemed sound in theory. Unfortunately, it worked poorly in practice. There was a tendency for a few students to monopolize the patients, while others waited impatiently for their turns. The session became protracted and confused. Reluctantly I abandoned this effort, and since then the clinical teaching has been more satisfactorily covered by assigning the students to the out-patient department in groups of five students to one instructor. Each new patient is assigned to a student, who takes the history, makes his examination, and, when possible, reaches his diagnosis. When this is done, he takes the patient to the instructor for review and discussion. At the conclusion of the session, each instructor assembles the most interesting patients of the day and holds an impromptu clinic for his own group, in which each student has the opportunity to examine these patients and discuss them with his instructor.

The next major question to be decided before actually formulating the didactic lectures, is when the course in ophthalmology should be given, and how it should be fitted into the medical curriculum. This is usually decided by a curriculum committee. However, it is the duty of the professor of ophthalmology to speak up boldly before this committee, to present a logical case, and to demand his proper place in the sun. If he does so, he is vastly more likely to get a good assignment than he will if he remains silent!

In many medical schools a course in diagnostic methods is given towards the end of the second year as an introduction to the clinical teaching. Included in this course should be instruction in ophthalmology. This instruction should be given to small groups and should be limited to demonstrations of the proper objective examination of the eyes, the determination of visual acuity, the use of the ophthalmoscope, and elementary perimetry. With this preliminary instruction, the student can forthwith begin to examine the eyes of his patients in the various dispensaries and the public wards. Here he will see things he does not understand, but they will awaken his interest in ophthalmology.

The actual course in ophthalmology should begin in the third year, and as early in the year as is possible. Ophthalmology should get away on an even start with the other branches of clinical medicine. The clinical dispensary instruction to small groups should preferably be entirely in the third year, and evenly distributed throughout the three trimesters or the four quarters. Since the clinical instruction of the small groups should not precede the formal instruction, the didactic lectures, which are whole class exercises, should ideally begin in the first quarter or trimester, as the case may be. As many as possible of these lectures, certainly the first twelve and probably the first sixteen, should be given in the third year. Thus the student will receive the bulk of his instruction in ophthalmology in the third year, and he will be able to employ this knowledge in his clinical work on the public

wards in his fourth year. Moreover, if the student is exposed to ophthalmology in the third year, before he finally decides on the branch of medicine he wishes to enter and makes application for an internship in the same, there is a thoroughly good chance that he may select our specialty. When ophthalmology was given almost entirely in the fourth year, I had many students tell me that they wished they had had earlier some intimation of how fascinating ophthalmology actually was. Had this intimation reached them in the third year, before they had made their decisions for other services, they might well have applied for ophthalmology. They were exposed to ophthalmology too late. Therefore, both because the student needs some knowledge of ophthalmology to use during his fourth-year ward work, and for the recruitment of future ophthalmologists, it is best to have the major part of the instruction in the third year. The fourth year lectures can best be devoted to advanced ophthalmology, to neuro-ophthalmology, and to review.

Having reached decisions on the general subjects to be covered, and how and when ophthalmology should be taught, the teacher is now confronted with the task of writing and organizing his didactic lectures. These are the backbone of his course. Exactly what specific subjects should be discussed, how extensive should the discussions be, and what should be the sequence of the lectures? I confess I do not know the answers to these questions. In the thirty-six years I have been charged with clinical teaching, I have reorganized the course a dozen times, have changed the content of lectures, and have repeatedly altered the sequence—and I am still uncertain and dissatisfied with the results. All I can do now is to tell you the pattern finally used when the time came for me to retire.

If there are twenty-four required hours available for formal didactic instruction in ophthalmology, I should suggest that approximately eight hours be assigned to instruction in what might be termed "straight" ophthalmology, i.e., the anatomy and physiology of the eye, exogenous infections, injuries, and the major intrinsic ocular diseases. The balance of the available time I would devote to instruction in the ocular changes which result from systemic disease, and to neuro-ophthalmology. Were a greater number of hours available for this formal didactic instruction, I would not increase the number assigned to the teaching of "straight" ophthalmology, but would devote the additional time almost entirely to medical ophthalmology.

In planning such a course of didactic instruction, I must reluctantly admit that I have found it necessary to give two preliminary lectures on the anatomy and physiology of the eye before beginning the clinical ones. While these subjects have already been covered in the preclinical years, they have not been covered from the standpoint of the clinician, and the material is not fresh in the student's mind. I have tried the experiment of omitting these lectures, only to find that the student is later confused through an ignorance of terminology and basic anatomy and is unaware of the clinical importance of certain physiological principles. However, because these lectures are necessary, they need not be dull. They should be made as interesting as possible, the clinical significance of anatomical points and physiological reactions stressed, and fine details glossed over. Moreover, the lecture on physiology affords a splendid opportunity for disposing of the subjects of errors of refraction and muscular imbalances!

The remaining twenty-two hours of didactic lectures are distributed over the third and fourth years. I believe the ideal arrangement is a total of sixteen lectures in the third year and eight in the

fourth, but I will settle for twelve and twelve. After we have assigned the first two hours to anatomy and physiology, what specific subjects shall be discussed under the five general headings already decided upon? I should suggest a program somewhat as follows:

A. The Reaction of the Eye to Exogenous Infection and Insult—three lectures. Suggested topics are, first, infections, inflammations and common diseases of the lids, lacrimal apparatus and conjunctiva; second, common diseases and infections of the conjunctiva, cornea, and sclera; third, injuries and burns of the eye and sympathetic ophthalmia.

B. The Common Intrinsic Ocular Diseases—three lectures. One each on cataracts, glaucoma, and the degenerations. Motion pictures of a cataract extraction and filtering operations can well be shown with the cataract and glaucoma lectures.

C. The Reaction of the Eye to Metabolic Disorders and Systemic Diseases—four lectures. Suggested topics are one lecture on exophthalmos, retrolental fibroplasia, deficiency diseases, etc.; a second on the ophthalmoscopic diagnosis of vascular sclerosis; the third can be devoted to the ocular changes of diabetes and the blood dyscrasias; the fourth can be on retinal diseases and a classification of the optic neuropathies.

D. The Reaction of the Eye to Systemic Infections and Hypersensitive Disease — seven lectures. Five of these I would devote to the subject of endogenous uveitis. According to the manner in which the lecture hours are divided between the third and the fourth years, several of these may go over into the fourth year. The first two of the uveitis lectures should be elementary ones on the classification, symptomatology, pathogenesis and general pathology of inflammations of the anterior uvea, and inflammations of the posterior uvea. The third lecture can well be devoted to the symptomatology and special pathology of specific forms of uveitis, while the fourth lecture should be on the subject of the etiologic diagnosis, and the fifth on the specific and nonspecific treatment of uveitis. Ocular syphilis and ocular tuberculosis can well be the subjects of the last two lectures of this group.

E. Neuro-ophthalmology—three lectures. Suggested topics are, first, the optic neural pathways and topographical diagnosis; second, the optic neuropathies, inflammations and atrophies; third, the ocular changes produced by intracranial diseases and tumors. As already stated, these formal lectures can profitably be supplemented by a series of elective clinics.

F. Reviews—two sessions. Reviews of fundus lesions can be made both profitable and highly interesting by the simple device of gathering up a number of unselected slides of various fundus lesions. These are shown at random, and a student is asked to describe what he sees as though he were dictating a note for a history. He is then asked his diagnosis. Other members of the class are asked if they agree or can add anything. It becomes an open seminar. When the resources of the class are exhausted, the instructor then describes what he sees and gives his diagnosis. Finally the diagnosis on the slide is read by the operator of the projector. The students enter into this game with enthusiasm, and these reviews are by far the most popular exercises of the year. They are especially enjoyable if the instructor plays fair with the class and goes into the review ignorant of the material to be shown. Nothing delights the class so immensely as the occasional time the teacher is wrong and one of the students has guessed correctly!

Each didactic lecture must be carefully adjusted for architecture, content,

and time of delivery. The absolutely perfect lecture has yet to be written. No lecture is ever so good that it cannot be improved upon. The common faults are poor design—putting on the superstructure before the foundations are complete, and putting too much in a single lecture. (A lecture is much like a thirty-foot boat—if you have one thing you cannot have another.) Yet it is amazing how much can be covered if the architecture of the lecture is good and if extrinsic aids are properly used. The most important of the extrinsic aids are a syllabus of the lecture, which should be given to the student, and the illustrative slides. The syllabus is valuable because the student is thus largely relieved of the necessity of taking notes, which makes it possible for him to devote his entire attention to the subject matter and the illustrative slides. The use of illustrative slides should include the free use of "dummies." These are short, typed headings or summaries. They hold a lecture together and ensure an orderly presentation of the subject. They promote clear thinking, and one cannot have a clear presentation without clear thinking on the part of the teacher.

The sequence in which the lectures are given should be adjusted according to the position of the course of ophthalmology in the general curriculum, and the students' schedule. Thus, if the ophthalmology lectures start at the beginning of the third year, when the student is first embarked on the glorious adventure of clinical medicine, I should be greatly tempted to lecture first on the reactions of the eye to the various systemic infections, intoxications, and metabolic and hypersensitive diseases, and to postpone the lectures on exogenous infections and the intrinsic ocular diseases until the end of the course. On the other hand, if instruction in ophthalmology does not begin until the last quarter of the third year or some time in the fourth year, I should probably follow the more conventional sequence already outlined. There can be no hard-and-fast rule. After the ophthalmologist has been assigned his hours, he should adjust his course in them so that it will be of the greatest interest and value to the student.

I have already alluded to the subject of elective courses in ophthalmology. Most of these courses are designed for men who do not contemplate becoming ophthalmologists but who, nevertheless, feel the need or have the desire for additional training. To this end, additional opportunity for work in the out-patient department and on the hospital wards should be afforded. Within limits, undergraduate students may be admitted to the courses in pathology, advanced physiology, chemistry, etc., which are designed primarily for the graduate house staff. There is, however, one elective in ophthalmology which is peculiarly adapted to undergraduate students, and which is well worth the labor and trouble of giving. This is an elective course in advanced medical ophthalmology. It should follow the required third-year lectures and should be open to third-year and to fourth-year students. If there are sufficient hours available in the required course, it can well be incorporated there, and made an integral part of the instruction in ophthalmology. In these lectures the ocular complications of such diseases as sarcoidosis, brucellosis, the collagen diseases, toxoplasmosis, syphilis, and tuberculosis can be explored, and the fascinating stories of their development unfolded. New developments in ophthalmology can be taken up and presented while they are still hot and in the formative stages—such subjects as the use of the adrenal cortex steroids, bacterial hypersensitivity, and the new concepts in the pathogenesis of diabetic retinopathy. In the twenty years I have offered such an elective, the content of

the course has completely changed. Not one of the original lectures has survived in anything like its original form! And I prophesy that if someone else continues this course, in another twenty years not one of the present lectures will be represented in the 1975 edition! Such a course has proved highly popular with the students, and it is almost as much fun for the professor as it is for them.

Such are my present somewhat amorphous views on undergraduate education in ophthalmology. I believe the available time should be equally divided between clinical instruction and didactic lectures. The clinical teaching should be with small groups of students in the out-patient department, with patients assigned to the student for examination and diagnosis. The didactic lectures should be carefully planned and organized exercises for the entire class. The required courses should be liberally supplemented by electives.

When I first began undergraduate teaching thirty-six years ago, I was dissatisfied with the accepted methods then in vogue. When I had the authority and opportunity, I changed the entire pattern of the teaching; when I retired last July I was still changing it. I am still not content, but I am less dissatisfied than I was in the beginning, and I am confident that we have made some progress. Further, I am sure the improvement in our teaching standards will continue, for pedagogy should never become static. And I am also sure that there will never be a universally accepted standard. There should be none, for teaching is a wonderful joy and should give to its disciples an opportunity to express their own personal convictions.

DISCUSSION

DR. RUEDEMANN: I wish to take this opportunity to thank Dr. Woods for his most excellent, comprehensive talk. It is very timely because many men are trying to find out how time can be obtained, in the first instance, and, in the second instance, what to do with it after they have it.

I think this lecture, if Dr. Woods has no objection, should be put in reprint form.

In the time that remains I think that we might have some expressions and questions from the floor. Dr. Woods will be glad to discuss them with you, because I am sure that in his thirty-six years, he has had experience in all the problems involved in obtaining time for teaching ophthalmology and in how to make use of it.

BRUCE F. FRALICK, M.D., Ann Arbor, Michigan: I certainly enjoyed the discussion and agree thoroughly that it should be available in reprint or published form. This section has not in the past taken advantage of the opportunity to publicize the worth-while information given here. This is a well conceived paper, written by a man who has probably had more years of experience than any of us attending. It shows that he has a definite interest in self-analysis, and through self-analysis has found the defects in his teaching and made a definite effort to improve. I feel that I have profited greatly by the discussion.

DR. RUEDEMANN: I might ask this question: Do you have any trouble with the curriculum committee as to getting time?

DR. FRALICK: We always wish we had more time, but recently we were given more time only by getting one of our staff members on the curriculum committee. Only by constantly fighting for adequate time are you going to be able to present ophthalmology to the undergraduate in a maner that will stimulate the better students to select our specialty.

DR. RUEDEMANN: In discussing this with Dr. Cordes yesterday, I made the statethat the men are complaining about not getting sufficient time for lectures, and Dr. Cordes immediately said, "In the places where we have been, our experience has been that most of the men do not make much use of the time allotted to them."

FRANCIS ADLER, M.D., Philadelphia, Pa.: I wish Dr. Woods would send me some of his courage to stand up and demand things of the curriculum committee, because we don't always get what we ask for.

Two changes are taking place which we must make note of in planning our curriculum, because we cannot tell any curriculum committee just what we in ophthalmology believe the students should have. This has to be planned in the light of our present philosophy

of teaching. The changes which are taking place, to which we must adapt ourselves, are:

(1) The didactic lecture is being done away with. Up until last year I had 37 didactic hours of teaching. For the last two years they have been cut down to 10. That is an enormous cut in lecture hours. Although there has been some increase in the hours of clinical instruction to substitute for the loss of lecture hours, the increase has been minimal.

(2) Our teaching must be adapted to the general practitioner. At least, the school I teach in has changed its philosophy, and everything is being built around the idea of general practice. That means we have to find out what the general practitioner needs from ophthalmology, and teach only that.

The scheme which has been adopted, which works beautifully on paper, in the Medical School of the University of Pennsylvania, is as follows: The course begins in the first year with correlation lectures that are supposed to show the student how the basic sciences of anatomy, embryology, chemistry and physiology fit in with the clinical years. In ophthalmology, this consists of one lecture in this correlation course while the student is studying brain anatomy. At this time we give them a lecture showing how the application of knowledge of the visual pathways helps the ophthalmologist and the neurologist to diagnose lesions in the brain. When they have their work in pharmacology, we give them a correlation lecture on the pupil, showing them how the neurohumoral theory fits into our conception of reaction of the pupil in physiology and pharmacology. In the second year, the students are assigned to the ophthalmology department for their work in physical diagnosis, and it is during that period that they learn how to use the ophthalmoscope and how to examine an eye generally.

We do not see the student again until the fourth year. I agree with Dr. Woods that it would be preferable to have the students in the third year—for only one reason, however. Although they are better trained in the fourth year, when they come to us, by that time they are so blasé that we have a hard time convincing them that they have anything to learn.

DR. RUEDEMANN: You have no hours in the third year?

DR. ADLER: None at all. As I stated before, we have them in the fourth year for lectures, and then also in the clinic. You may recall that I advisedly stated that this works out well on paper. The plan which we are now running on is to assign a patient in the out-patient department to a student. If the patient happens to have an eye consultation, the student follows him to our clinic. Let's say that student A has a patient who has hypertension. Obviously part of a work-up on that patient in the out-patient department will be an eye examination. The student comes to us with the patient at an appointed time, and he sees what our diagnosis is. He looks into the eye grounds after we have, and so on. His next patient may never come near the eye department, however, and since all his contacts with us are only through his patients, his knowledge of ophthalmology depends somewhat on chance, that is, how many patients he may get assigned to him during the year who eventually reach the department of ophthalmology. The emphasis, you will note, is not on any vertical structure in the medical school, so that each department is separate, but on the cross-sectional structure; from the point of view of the general practitioner, this is probably as it should be.

You can see that this is fine on paper, but it is still full of difficulties which have to be solved. In the first place, some of the students get to us very often, whereas other students may never come to the eye department. Some students may get a run of diabetics, and other students may never see a diabetic fundus. Another practical difficulty is that the student brings the patient in for an appointment, but it is seldom that these appointments can be kept promptly in any clinic, and so the student may lose some time.

These are some of the changes which we have to adapt ourselves to, and we must build our course around the main medical curriculum.

MEMBER: Dr. Adler, do you feel that having lost a certain number of the didactic lectures, the time is lost, or do you think the clinical groups are better?

DR. ADLER: I think we need more lectures. We need a minimum, I would say, of twenty lectures.

DR. RUEDEMANN: Dr. Adler's idea of correlation lectures is very good.

DR. WOODS: We have those lectures, too, but they consist of one of the instructors going over and lecturing to the students in anatomy during that part of the course in anatomy.

EDWIN B. DUNPHY, M.D., Boston, Massachusetts: I think there is very little I can say in discussion of Dr. Woods' paper because I agree with practically everything he has said. All I can do is emphasize certain points that he made.

The first one is that we should not try to teach too much if we are limited in time. Don't feed the student more than he can absorb. Dr. Woods and I were on a committee in 1948 which drew up certain minimum standards of instruction in ophthalmology on the undergraduate level. I remember a term that we used, and I think he coined it: "Don't try to show the student the anomalies and curiosities of medicine in the short time at our disposal."

Another thing we should do, as he has already said, is to assume that these students are going to be general practitioners; therefore, try to teach ophthalmology from the standpoint of general medicine rather than in a little cubbyhole by itself.

I, too, like Dr. Adler, wish that we had Dr. Woods up at Harvard to do some straight talking to the curriculum committee, because in our third year ophthalmology we have a total of only 40 hours of instruction, five of which are didactic lectures. Being limited to only five lectures, it is foolish to try to cover the whole ground. I cover only certain subjects and, incidentally, these subjects are more or less those which Dr. Woods spoke about, broad general subjects related to general medicine.

If we are forced to limit ourselves, we should try to get the cooperation of the other departments; see if we can steal a little time from them unofficially. We do it. In the first year, a member of our department lectures an hour in anatomy and another hour in physiology; he deals with the anatomy and physiology of the eye at the first-year level in those departments, likewise, in the second year, we have an ophthalmologist who gives an hour on pathology of the eye in the pathology course.

In the latter part of the second year, when the students are exposed to clinical medicine for the first time, I used to have the scheme of dividing the class into four quarters, each quarter containing about 30 students—and I gave them instruction on the use of the ophthalmoscope. No attempt was made to show them any pathologic conditions whatsoever. I just simply got each student to look in the eye of his fellow student and to identify the disc and blood vessels. This was valuable to them, but now unfortunately this time has been taken away.

We do have one other lecture in the second year on the relation of the eye to general medicine. This is an orientation lecture, but I do not think it has the practical value that the exercise on the ophthalmoscope had.

I enjoyed hearing Dr. Woods very much, indeed, and feel that he has pointed out some ways in which the undergraduate instruction in ophthalmology can be improved.

ALBERT LEMOINE, JR., M.D., Kansas City, Missouri: At the University of Kansas we are primarily interested in the general practitioners because we are a state school in a predominantly rural area. We have the same problem with reference to the hours allotted for ophthalmology, and we are now tentatively considering a scheme that I think has possibilities and also some drawbacks.

In the senior year we have sections, of about twelve students each, four times in the Eye Out-Patient Department. These periods in the eye department are for three hours. During the junior year we have eighty periods of one hour each for didactic lectures, with the entire junior class in attendance.

The scheme that we are considering is to have one member of the Department of Ophthalmology attend the weekly rounds on medicine, pediatrics, neurology and neurosurgery. The plan would be for the ophthalmologist to discuss the eye findings and basic pathology of the patients with ocular involvement on the other hospital services. These rounds would be attended by the students and members of the specialty service.

It would appear that this program would be of help in the integrated teaching plan and should aid in considering the patient as a whole. The disadvantage would be the loss of identity of the eye department, as such, in this program.

This program is similar to that discussed by Dr. Dunphy, in which one steals time from other departments.

DR. RUEDEMANN: Dr. Woods, have you anything to say?

DR. WOODS: I think integrated instruction is splendid for postgraduate teaching or graduate teaching. Let us, however, differentiate between undergraduate, graduate, and postgraduate teaching. Graduate teaching is the training of ophthalmologists, and postgraduate teaching is what we do here at the Academy.

Nothing is more valuable than to invite the allergists, the internists, the psychiatrists, and the urologists over to your wards to make rounds with you when there is interesting material in their fields. This is of tremendous value to the staff. This is difficult to do with undergraduate students. They have a crowded curriculum. They have only so many hours, and they have to go from one thing to another. I sympathize with the undergraduate.

He goes from gynecology to urology, to psychiatry, to otolaryngology, to ophthalmology—those are all shoved down his throat, and the poor fellow's head is spinning. It is hard to fit integrated instruction into class exercises. It can be done with group exercises for individual groups, but then one student gets a type of instruction that the others do not.

It is almost impossible to give an organized and uniform course and to cover the material you want to cover if you rely on clinical material alone. When you ask guest speakers to come in and discuss a patient, you are dependent upon the availability of clinical material. We cannot depend upon a proper flow of clinical material to teach the essentials of ophthalmology.

HAROLD F. WHALMAN, M.D., Los Angeles, California: We all immediately recognize that we are up against two conflicting issues: one, getting enough hours alloted to present our subject and the other recognizing that a lot of information from all departments has to be crowded into a limited time.

At the College of Medical Evangelists we are alloted ten didactic hours in the junior year, with clinic group-teaching in the senior year and assignment to Eye Clinic for a period during the intern year. I believe twenty-four didactic hours to be excessive in the light of a heavy general schedule.

From the student's viewpoint, a lot is going to depend upon the personality and presentation of the professor. If he stands before the student as strictly a specialist, the cause is lost, but if he can intrigue the student, making him understand that ophthalmology is not a narrow limited specialty but is broadly related to the entire field of medicine, he will capture the interest of the student, who will then seek the aid of the eye department throughout his medical training.

I think that this address of Dr. Woods, and whatever part of the discussion as seems desirable, should be published for the sake of presenting our viewpoint to our respective deans and department heads.

MEMBER: I should like to ask Dr. Woods what he has found with respect to using the residents to teach the students in the clinic. How successful has it been in his experience?

DR. WOODS: I should say it has been very successful. The assistant residents are good men. They have had two or three years of training. They have had the viewpoint of the student and still remember it. I think such instruction has been highly successful.

I should like to say one thing with reference to the remarks made by Dr. Whalman and some of the other gentlemen relative to the number of hours that should be allocated to ophthalmology. There are 5,000 hours in the whole medical curriculum, and about 2,500 hours in the last two years for clinical instruction. Medicine and surgery are, of course, the backbone of medicine, and you have to put at least 600 or 700 hours apiece into medicine and surgery, and probably more if you are going to train a doctor. That does not leave you much more than 800 or 1,000 hours altogether to teach ophthalmology, psychiatry, pediatrics, genito-urinary diseases, otolaryngology, orthopedics, neurosurgery, and all the other things.

How much can you put in? Frankly, I don't believe that ophthalmology should have over 75 hours. I believe that we should certainly have a minimum of 40. I do not think you can come anywhere near covering your course in less than 40 hours. Up to this year we have had 48. At Johns Hopkins the curriculum was reorganized this year. Instead of getting 24 clinical hours, we got 36 clinical hours and the same 24 didactic hours. In other words, our allotment of hours was stepped up to 60. I asked for 68, so that the medical ophthalmology course could be sandwiched in between the third and fourth years. I did not get that. However, they gave us some intimation that we might get these additional eight hours in another year.

It is true, as I said, that if the professor of ophthalmology will stand up and present a logical case to the members of the curriculum committee, he will find them amazingly sympathetic, and he may get a good deal more than he thought he would at first.

DR. RUEDEMANN: Your last point, Dr. Woods, with regard to working with the other departments, is very interesting in that some of the other departments are very happy to have the ophthalmologist come in and take some of their lecture time, and it works out very well. Evidently some of them have a little more time than they need.

If you will critically analyze the curriculum of the medical school, you will find that in the first two years all the professors have taken all the time they could get, with the idea in mind that they are building up their own departments. If you will go to them and try to analyze it realistically with them, they will admit that they could get along with an hour less here and there.

I think that the sixty hours of instruction that Dr. Woods has outlined is the minimum if you are going to teach ophthalmology—even to the general practitioner.

Are there any other questions?

ALFRED KESTENBAUM, M.D., New York City: I should like to ask Dr. Woods if it would not be wise to add to the chapters he mentioned, a chapter on the indications and prognosis of ophthalmic surgery, because patients ask their general practitioners whether they should be operated on or not. I think it would be well for the general practitioner to know a little about the worth of retinal detachment operations, strabismus operations, and so on.

DR. WOODS: I agree with you, Dr. Kestenbaum. When you are talking about diseases of the retina, you should tell the students that previous to 1929, there was practically no treatment for detachment of the retina. Since then operative means have been devised and have gradually been improved upon until now we have a reasonably satisfactory operative approach for detachment of the retina. This lies in the formation of chemical choroiditis—adhesions between the choroid and the retina. That is all you need to say.

The same thing applies to squint. There is no use trying to teach students muscle anomalies. They should know the meaning of esophoria, of exophoria, and of hyperphoria. That is all they will ever remember, and it is foolish to take the time to try to teach them anything more.

A motion picture of a cataract operation is spectacular, but it is complicated. You can say to the students, after they have seen a motion picture of the operation, "If you would like to see a cataract operation, come up to the operating room, there is one being done every day." They will come if they are interested.

To put it into one phrase, we cannot teach the special disciplines in an undergraduate course. We do not have the time. I would like to, but I cannot.

ROBERT J. BILLINGS, M.D., Pittsburgh, Pennsylvania: We have been talking about the direct instruction of the students. How about the indirect work that the student is supposed to do in looking up material? We have gone through a process of change in the University of Pittsburgh from the didactic type of teaching to the conference type, or the ambulant type, with a small group of students coming in. So, in order to save time and to have them become acquainted with the varied subjects, we assign the students individual problems to look up themselves, for instance, hemorrhages of the eye, or internal eye conditions, and then to give a 15-minute or 20-minute dissertation to the group of maybe eight students and the professor, who sits in on the discussion of the problem. We find that we can cover more conditions that may be coming through the clinic in that way.

DR. WOODS: I would have to disagree with that, doctor. What does a student get? He talks to a group of students for fifteen minutes on the subject of retinal hemorrhage. Sometimes he passes out misinformation. I think that in graduate teaching nothing can be better than seminars, the allocation of a subject to a student: the man in training for ophthalmology learns how to study a subject, how to analyze it and present it. Let his presentation be criticized in an open seminar and don't bother about his feelings. Straighten him out, and teach him to do better! In my experience it has been of little value to assign home exercises and homework to the undergraduate student. There is so much he has to study—to review all of his cases, to look up and read. If he confines his reading in ophthalmology to looking up the cases he saw in the dispensary that afternoon, it is all one can ask. You cannot assign to him an exercise; he will do it indifferently and get nowhere with it. It is the duty of the professor, in my opinion, to outline the elementary work that should be covered and to encourage the student to seek help. The professor should have his door wide open and invite the students to come and talk to him about anything they like.

BERNARD FREAD, M.D., New York City: We do the same thing at the New York University Medical College, where Dr. DeVoe and I try to preserve our few hours of teaching. We have only five didactic lectures during the four years. During the first year a lecture is given on anatomy and physiology of the eye to correlate our work with the general course in those subjects.

During the second year, we give three formal lectures in ophthalmology. The second-year course is part of the studies in general physical diagnosis, and we try to cover the physical diagnosis of the eyes as part of that course. We divide the entire class of about 130 students into groups of ten, subdivided into groups of five, and each group of five has an individual instructor. The classes are held in the eye clinic, where the students are given clinical instruction in the use of the ophthalmoscope, in diagnosis, and particularly in the study of the normal human eye, both externally and internally.

In the third year we have no formal lectures, but we present two or three sessions in ophthalmology as part of the course in general medicine, in the medical wards.

During the last year, up until recently, we have tried to show specific cases in ophthalmology as part of a general survey; giving diseases in ophthalmology that we see in our clinic, and supplementing our clinical material with lantern slides.

Our faculty has just changed the fourth-year teaching to an elective. The students come in for two weeks at a time to our eye department and spend their time in the clinics and in the Bellevue Hospital Wards.

In summary, we have a total of five didactic lectures and 20 clinical hours. Students choosing ophthalmology as an elective have about sixty hours of intensive work during their fourth year.

At least we have preserved our integrity and our identity as the Department of Ophthalmology.

We certainly appreciate Dr. Wood's lecture and his philosophy of teaching. It has really been an intellectual treat to hear him.

RICHARD C. TROUTMAN, M.D., New York City: I noticed that Dr. Woods talked about the free use of visual aids. Many of us are severely hampered because our photographic departments do not supply sufficient visual aids. I wonder if the Academy might compile a list of visual aids that are available from medical schools that we might call upon.

DR. RUEDEMANN: I think you might ask Dr. Benedict directly. I am sure he would be very happy to spend the money. This is a good idea, and we will put the question through.

If there is nothing further to come up this morning I wish to thank you, Dr. Woods, for a most excellent morning.

RETURN ENGAGEMENT

The Clinics in Mexico postconvention tour, conducted in October 1955 by Mr. Leon Arnold, will be repeated in 1956. Through the courtesy of the chiefs of ophthalmic and otolaryngic clinics of the several hospitals in Mexico City, our members are again privileged to visit the five hospitals of Mexico and to observe at first hand the facilities and practices in one of the most progressive of the Latin American countries.

Brochures containing full information concerning the tour will be mailed to all members soon.

Read what two of the Fellows who went last year wrote about the Clinics in Mexico in the November-December 1955 TRANSACTIONS. For further information write Mr. Leon Arnold, Holley Chambers, 33 Washington Square West, New York 11, New York.

In Memoriam

Thomas Dyer Allen.....Evanston, Illinois
February 14, 1956

James Bordley, Jr.....Baltimore, Maryland
January 7, 1956

Edgar Osgood Breakstone.....Chicago, Illinois
November 3, 1955

David Nathaniel Husik.....Philadelphia, Pennsylvania
November 20, 1955

John H. Kincaid.....Hollywood, California
January 20, 1955

Adolph Krebs.....La Mesa, California
August 23, 1955

James William Lehan.....Greeley, Colorado
October 30, 1955

Tom Otto Walter Meissner.....Athens, Georgia
October 29, 1955

Samuel Archard Morris.....Los Angeles, California
December 3, 1955

C. F. Nutter.....Nashua, New Hampshire
December 22, 1955

Henry Paul Schugt.....New York, New York
January 30, 1956

William Hamilton Smith.....Hagerstown, Maryland
November 7, 1955

Peter Hunter Thompson.....Boston, Massachusetts
December 1, 1955

A. Charles Zehnder.....Newark, New Jersey
December 1, 1955

TRANSACTIONS

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William L. Benedict, M.D., LL.D., Executive Secretary-Treasurer,
American Academy of Ophthalmology and Otolaryngology,
100 First Avenue Building, Rochester, Minnesota

TEACHERS' SECTION

The following editorial prepared by the public relations office of the American Medical Association is a suitable introduction to a presentation of the program of the Academy, which for more than twenty years has placed medical education and instruction in ophthalmology and otolaryngology high on the agenda.

For several years the Academy has invited discussion of school problems in the Teachers' Section. Here prepared papers are read putting forth the existing conditions under which the specialties are taught in undergraduate medical schools and in graduate schools. Problems of curriculum, physical space, hospital beds, administration, intern and residency requirements and regulations, as well as clinical material, research and development of technical skills all come in for review in a free discussion of efforts to improve the professional proficiency of doctors who practice in the field of eye, ear, nose and throat.

The consideration of these problems has been a function of organized medicine, and many national societies make it a major item in their programs. There are many facets. A medical specialty is a block in a complicated structure. Its position and its function in the eyes of the architect vary with his objectives.

As the structure assumes shape and its functions are defined, someone must decide where each block shall be placed and what its relation to the structure shall be. All buildings are not alike. Architects have different objectives and various viewpoints. Some will make a block independent rather than a support for another. So long as there is freedom of choice among architects, there will be variability in structures. When freedom of choice is denied and blocks are placed under compulsion to provide uniformity, then dissatisfaction and resentment occur. There will always be such problems among medical school administrators and teachers. Even unanimous decisions are never completely satisfactory.

The Academy Teachers' Section is a forum for free speech. It is only one of many such. The difference is that the Academy discussion is limited to the fields of two or three medical specialties; the structure as a whole is the subject of another group. The American Medical Association covers the entire field of medical education and invites the public. The Academy joins in this nationwide observance. It has something to show.

MEDICAL EDUCATION WEEK
April 22-28

The medical profession and all allied medical personnel are being called upon to help promote the first nationwide observance of Medical Education Week, April 22-28. Each community, whether or not it includes a medical school, is requested to plan programs dramatizing the great progress of our medical schools in recent years.

Specifically, Medical Education Week has three functions: (1) to focus national attention on the significance of medical education and the problems of medical schools; (2) to bring home to the public the contributions of medical science to American life, and (3) to foster public interest, through wide public knowledge, in the private support of medical education.

The sponsors of the Week hope that the American people, through an awareness of the benefits received through the schools' achievements, will be converted from a disinterested — and sometimes hostile—public to appreciative friends of medical education.

By opening the doors of the nation's medical schools, both literally and figuratively, to public view, many of the false rumors and myths hampering United States medical education can be disproved. Too many Americans believe the schools are lagging far behind the national rate of growth by keeping a tight lid on enrollments, when, in fact, the academic year of 1954-55 was another all-time record breaker in both enrollments and graduates. Over the past half century the rate of increase of physician graduates has outstripped the rate of growth among the general population.

These facts and the dramatic success in the schools' laboratories will be directly related to the public—the beneficiaries of this progress—during Medical Education Week.

President Eisenhower, in giving his personal endorsement to the observance, said, "This Week will give the American people a special opportunity to learn of the great contributions to the national welfare which American medical schools have made, and the goals which they have set themselves for the future."

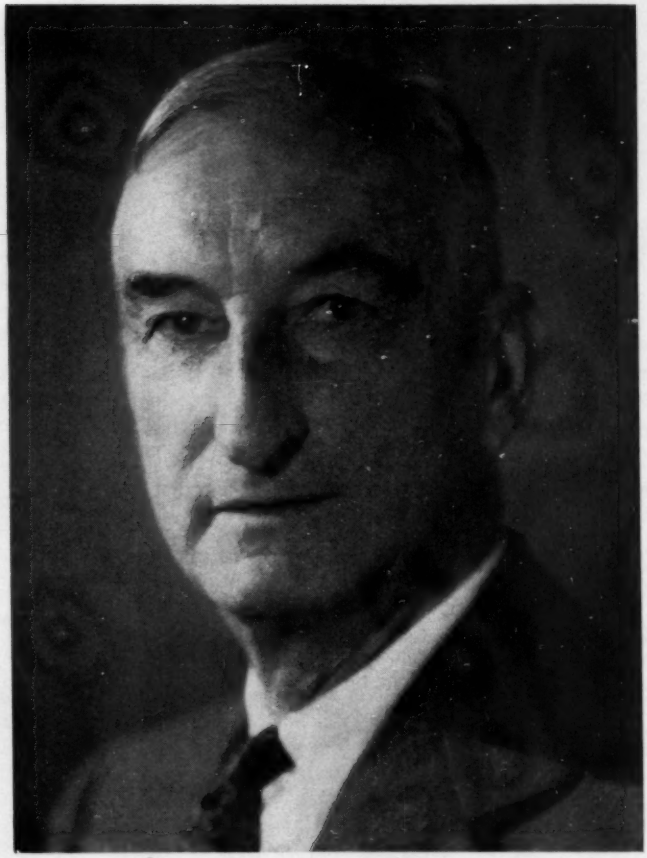
All of the sponsoring organizations—the American Medical Association and its Woman's Auxiliary, the Association of American Medical Colleges, the Student American Medical Association, the American Medical Education Foundation, and the National Fund for Medical Education—are enlisting the cooperation of their memberships to help tell this story.

At the national level, these organizations are providing promotion through syndicated news features, magazine articles, and network radio and television programs.

Most medical societies throughout the country have already appointed chairmen for their respective community coordinating committees and they are therefore prepared to welcome your assistance in building programs for Medical Education Week.

The success of this first observance depends on the cooperation and help of everyone in the field of health and medical care.

In Memoriam



JOHN MACKENZIE BROWN, M.D.

1878 - 1955

JOHN MACKENZIE BROWN, M.D.

1878-1955

John Mackenzie Brown was born in London, Ontario, Canada, in 1878. He received his preliminary education and was graduated from medical school at the University of Western Ontario in 1899. Shortly thereafter, he decided to come to the Southwest and made his permanent home in Los Angeles at the turn of the century, becoming an American citizen within a few years. Becoming interested in otolaryngology early in his career, he decided to obtain special training in this field and traveled extensively, studying at the University of Michigan, University of Pennsylvania, Harvard University, University of Edinburgh, and at several European centers.

His skill in his special field was quickly recognized, and he was appointed to a number of hospital staffs in Los Angeles. He was one of the first members of the staff at Children's Hospital, and remained active in that institution from 1909 until 1955. He served not only as Chief of the Department of Otolaryngology but also as Chief of Staff at that hospital for a number of years. He maintained affiliations with many other hospitals in the city, including St. Vincent's Hospital, the Eye and Ear Hospital, Hospital of the Good Samaritan, and the Cedars of Lebanon Hospital. His services as a consultant were constantly sought at these and other hospitals.

With the re-opening of the School of Medicine at the University of Southern California in 1928, Doctor Brown became vitally interested in the welfare of this institution. He became Professor and Head of its Department of Otolaryngology in 1930. Several years later he became Chief of the Department of Otolaryngology at the Los Angeles County General Hospital, and even after his promotion to Professor Emeritus in 1950, he maintained an active interest in the work of both institutions.

The Residency Training Program and the Postgraduate Education in Otolaryngology were greatly stimulated and put on a solid footing during his period of leadership. His Wednesday rounds at one o'clock became traditional at the County Hospital and were renowned throughout the country for their excellence and stimulation.

Doctor Brown was deeply interested in the national otolaryngological societies, and served as an officer in many of them. In addition to serving as President of the American Laryngological, Rhinological and Otological Society, and President of the American Academy of Ophthalmology and Otolaryngology, he was also a member of the Los Angeles Society of Ophthalmology and Otolaryngology, the Pacific Coast Oto-Ophthalmological Society, the American Otological Society, and the American Laryngological Society. He was a devoted member of all of these organizations and rarely failed to attend a national or local meeting of any society in the field of otolaryngology.

During his many years in the practice of otolaryngology, Doctor Brown contributed much to the advancement of the specialty, and his contributions in several fields are world famous. His work on the frontal sinus, including his advocacy of early trephine in acute frontal sinusitus and conservative surgery in chronic frontal sinusitis; his work in branchial-cleft anomalies; and his interest in intracranial complications were well recognized throughout the world. He served as Associate Editor of the Archives of Otolaryngology for many years.

But all of these sterling qualities and great accomplishments in the field of medicine do not tell the real story of "J. M.," a truly beloved physician. He will be remembered by many thousands of patients who knew him as a kind and able physician with real devotion to the sick. To his fellow physicians, he was known as an astute diagnostician, and a very able surgeon in the field of otolaryngology. To many otolaryngologists now practicing, not only on the West Coast but in various parts of the country, Doctor Brown will always be the great teacher, the great educator, and the kindly advisor who guided and helped innumerable young men in the specialty of otolaryngology. He was deeply interested in people and in education. He was a strong guiding force in the early days of organization of the School of Medicine at the University of Southern California, and for many years was a member of the executive committee of the faculty. A large group of his former students and friends have for years met at the annual meetings of the American Academy of Ophthalmology and Otolaryngology as the "John Mackenzie Brown Alumni Group," and have awarded an annual recognition to that member of the group who made the best contribution to the literature in that year. This award is considered a great honor. In 1949, a testimonial dinner was given to Doctor Brown by a large number of otolaryngologists in the Southern California area upon the occasion of his completion of fifty years of practice. At this testimonial dinner, an oil painting was presented to him by his devoted friends, and copies of this painting hang in many otolaryngological offices on the West Coast.

"J. M." was a most humble and modest person who always tried to remain quietly in the background. Nevertheless, his great character and human qualities were so evident that many honors were presented to him during his years in practice.

Remaining actively engaged in practice and in his educational work until the very end, Doctor Brown passed away in his sleep on December 31, 1955. He is survived by his widow, Marian, two daughters, two sons, and six grandchildren.

The John Mackenzie Brown Memorial Fund has been established to perpetuate the name of the man who was known as the dean of otolaryngologists on the West Coast, and who made contributions to the specialty which will be permanent in the archives of the specialty. This fund will be used to build a lecture hall in the new University of Southern California Medical School Center. This will be a fitting memorial to Doctor Brown, who was very anxious to see education in medicine raised to the highest possible level.

INTERNATIONAL ASSOCIATION OF SECRETARIES OF OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETIES

PROGRESS IN MEDICINE

In medical science the formation of an "elite" is indispensable for the progress of scientific research and for the evolution of scientific medical thought. Unfortunately, this problem has been neglected everywhere because society has become more and more preoccupied with social matters and less with intellectual ones. Continuous preoccupation with a material future world leaves no time for intellectual problems which, in a way, are too abstract, too far removed from life.

In medicine, especially, much depends on practical activities, on studies made exclusively for utility. And yet significant progress is largely dependent upon intuitive understanding and honest assessment of human values. Man tries to nullify himself by enlarging the power of the State and by becoming absorbed in it. Thus he rebels against his destiny, against that which he bears within himself as a divine gift.

The evolution of contemporary medicine certainly does not encourage great expectations for the future. It is preoccupied with socially standardized performance. The opposite should be true. Individuals of high culture should be selected, men in love with research, physicians of inventiveness and intuition. A cycle of evolution should be created and continued uninterruptedly: a succession of physicians with high cultural and spiritual aims. Ideas and systems of thought should be carried from a Master to the pupil, and continued by the pupil in the position of a new Master. This task cannot be undervalued, particularly by those who draw from the study and practice of medicine the comfort as well as the torment of a high and beneficial spirituality.

I want to believe that the International Association of Secretaries of Ophthalmological and Otolaryngological Societies can make an important contribution. This organization should work toward the increase of "inter-exchanges" of information and of contacts of groups of physicians within its specialties in all parts of the Free World. It should, in addition, study and discuss plans for selective cultural and scientific activities of sectional, national and international societies.

The activities of national and international congresses should be aimed toward the selection and the formation of an "elite." Much effort should be expended to encourage clear and prominent individualities, especially among the younger ophthalmologists and otolaryngologists.

The choice of arguments, the tenor of discussion, and the friendliness of approach should create love of research, consciousness of deep scientific earnestness, and a sense of undeviating logical rigor. In many congresses one or the other of these aims has been found wanting, perhaps because of lack of interest. Vacuity of dialectic logic is not infrequent, and inconsistency of scientific sequence of procedure is often present.

The task is certainly arduous and difficult. But if we would like to see medical science progress, if it were our wish that society give a privileged position to those who seek self-improvement through study and research, then we

must face our task intelligently. We must try deliberately to find a solution, even though we know we may be economically below the level of income of a boxer or skilled laborer.

PROF. E. FILIPPI-GABARDI, M.D.
General Secretary, Latin Society of Ophthalmology

INTERNATIONAL SECRETARIES REPORT

ISRAEL OPHTHALMOLOGICAL SOCIETY

The Palestine Ophthalmological Society was founded in December 1925. In its present form the Israel Ophthalmological Society exists since 1951.

There are at the time 106 ophthalmologists in the country, practically all members of the Society. So far, there exist no fixed rules as regards specialization, but a committee is at work on a draft of appropriate regulations which will have to be approved by the Society and the University Medical School (Post-Graduate Studies).

Society meetings are convened four to six times annually and take place alternately in the ophthalmological departments of the five following hospitals: the Jerusalem University Hadassah Medical School Hospital, the Haifa Government Hospital, the Tel-Hashomer Government Hospital, the Tel-Aviv Municipal Hadassah Hospital, and the Jaffa Government Hospital.

During the last two years we have had a number of distinguished guests, most of them lecturing and presenting teaching films: Sir Stewart Duke-Elder, Dr. Milton Berliner (New York), Dr. Isador Givner (New York), Dr. Harvey Thorpe (Pittsburgh), Dr. N. Moura (Rio de Janeiro).

Apart from the activities previously mentioned, local chapters of the Society are active in Jerusalem, Tel-Aviv and Haifa, and meetings with clinical demonstrations and discussion of interesting cases take place regularly.

Research activities are concentrated at the Department of Ophthalmology at the University Hadassah Medical School Hospital in Jerusalem, on various pathological problems.

Also in Jerusalem is the Harry Friedenwald Medical (Historical) Library, which contains works on medical history, especially on ophthalmology, among them some very rare books.

I should consider it very advantageous if catalogues of ophthalmological films could be made available to us.

AMOS LAVYEL, M.D.
Secretary

OPHTHALMOLOGICAL SOCIETY OF EGYPT

The Ophthalmological Society of Egypt holds yearly two main scientific meetings, one in March in Cairo and the second in August in Alexandria. The Society also holds monthly meetings in October, November, December, January and February. These are evening meetings, in each of which a subject is discussed, and some of them are accompanied by surgical demonstrations.

There is an Ear, Nose and Throat Society in Egypt. Its Secretary is Dr. Aly El Mofti, Dar El Hekmah, 42 Kasr El Ainy Street, Cairo, Egypt.

SABRI KAMEL, M.D.
Honorary Secretary

SOCIETY OF THE NORWEGIAN OPHTHALMOLOGISTS

Our Society of the Norwegian Ophthalmologists (Norske oyenlaegers forening) has only two meetings a year, usually in Oslo. From the program:

Wiborg-Steen: Retinopathia hypertonica gravidarum, treated with Serpasil

H. P. Petersen: Malformation of anterior chamber

Ivar Haadem: Melanoma in the eye

Holst-Berg: Temporal arteritis

Hakon Leira: Meningitis and uveitis

DR. J. C. HOLST
Secretary

BARCELONA ASSOCIATION OF OTO-RHINO-LARYNGOLOGY

We are organizing the Xth International Congress for Speech and Voice Therapy, to be held in Barcelona, September 3-7, 1956.

In our country Ophthalmology is separated from Oto-rhinolaryngology. The Association O.R.L. is the oldest in our country. We have a meeting every month, with two or three lecturers each.

DR. J. PERELLO
Secretary

LATIN OPHTHALMOLOGICAL SOCIETY

The II Congress of the Societas Ophthalmologica Latina will be held in Madrid, Spain, April 24 to 28, 1956. The paper which will be presented to the Congress is: "The usage of acrylic material in ophthalmology." The paper will be discussed by Dr. H. Arruga (Barcelona), Prof. G. B. Bietti (Parma), Prof. L. Paufique (Lyon), Dr. O. Ferrer Paisan (Habana), Dr. Legrand (Nantes).

PROF. E. FILLIPI-GABARDI
General Secretary

THE OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

The Annual Congress of the Ophthalmological Society of the United Kingdom will be held at the Royal Society of Medicine, 1 Wimpole Street, London, W.1, on April 26 to 28, 1956.

Topics: "The Early Diagnosis of Glaucoma" and "Herpetic Infections of the Outer Eye."

The Annual Dinner will be held on Thursday, April 26, 1956.

Honorary Secretaries
Derek Ainslie, (*Council Business*)
C. A. Cook, (*Congress Business*)

CHILEAN SOCIETY OF OPHTHALMOLOGY

The officers of the Chilean Society of Ophthalmology (Sociedad Chilena de Oftalmologia) for 1955-1956 are: President: Dr. Alberto Gormaz B.; Secretary: Dr. Carlos Charlin V., Mac Iver No. 175, of. 24, Santiago, Chile.

Meetings are held the last Wednesday of each month at Av. Salvador No. 300, 7 p.m.

The next biannual meeting will be held at Valparaiso in November 1956.

DR. CARLOS CHARLIN V., M.D.
Secretary

BOOK REVIEW

SYMPOSIUM OF AUDIOLOGY. By W. H. Fitzhugh, Jr., M.D., V. W. Stacey, Inc., San Francisco, 1955, 77 pp., $2.50.

This small, loose-leaf book is published as a ready-reference work for the audiologist who needs rapid refreshment of the memory. It has a fairly adequate index and good bibliographic material. One noticeable omission is any reference to methods of estimating disability from hearing loss.

This book should prove a very useful rapid reference manual for those doing audiology.

H.L.W.

CHANGE OF ADDRESS

PLEASE NOTIFY the office of the Secretary of the Academy of change of address. TRANSACTIONS mailing envelopes are addressed three weeks before mailing date. Your copy will reach you if we have your correct address. Please keep us up to date on your CITY, ZONE AND ROOM NUMBER OF YOUR OFFICE BUILDING. TRANSACTIONS and DIRECTORIES are returned to the publisher each month because we have not been informed of changes of address.

The DIRECTORY is compiled once a year, in March. Check your name and address now to see if it is correct. If not, please notify the editor at once. Send us word immediately of any future change.

News - - - Notes

SIXTH INTERNATIONAL CONGRESS OF OTOLARYNGOLOGY

The Sixth International Congress of Otolaryngology will meet in Washington, D. C., May 5-10, 1957. Preliminary announcement was sent to every otolaryngologist of record in the world in early autumn, 1956, asking that those interested indicate this fact by returning an enclosed card. A second notice with further information will soon be sent to those who returned these cards. If you wish to receive the second announcement and the original one did not reach you or you did not return the card, please notify Paul H. Holinger, M. D., General Secretary, 700 No. Michigan Ave., Chicago 11, Ill., U.S.A. so that your name may be placed on the active mailing list.

AMERICAN BOARD OF OPHTHALMOLOGY
NOTICE OF CHANGES IN REQUIREMENTS

(Applicable to applicants who start residencies in ophthalmology after December 31, 1956)

Individuals who have completed three years of formal ophthalmological training (residency and basic science courses) may apply for the written qualifying test after completion of 12 months of practice or 12 months of institutional work, a total of 48 months. All other individuals (with less formal training) may apply for the written test after 60 months in ophthalmology or 72 months of combined ophthalmology and otolaryngology. A basic course is recognized as equivalent in time to residency training. ALL TIME REQUIREMENTS MUST BE COMPLETED BY THE DATE OF THE WRITTEN TEST.

AMERICAN ORTHOPTIC COUNCIL

The Basic Course in Orthoptics for Technicians, sponsored by the American Orthoptic Council, will be held in the Department of Ophthalmology, University Hospitals, Iowa City, Iowa, from June 20 through August 11, 1956. As usual, there will be didactic lectures and practical demonstrations, given by an outstanding faculty.

Further information and registration blanks may be secured by writing Hermann M. Burian, M.D., Department of Ophthalmology, University Hospitals, Iowa City.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, MIDWEST SECTION

The scientific session of the Midwest Section of the Association for Research in Ophthalmology will be held in Chicago on March 17, 1956, Room 407, Commerce School, Northwestern University, 321 E. Chicago Ave. The sessions begin at 9:00 a.m. and 2:00 p.m. Lunch will be served at the cafeteria in Abbott Hall, across the street. The program follows:

Julia T. Apter, Manteno, Ill.: Effect of Hallucinogenic Drugs on the Electroretinogram Studies on the Autonomic Innervation of the Iris

S. B. Goren and A. C. Krause, Chicago: Oxygen in the Vitreous Humor in Anoxia and Hyperoxia

I. Gersh, Chicago: Electron Microscopy of Ocular Tissues

K. L. Chow, Chicago: Disuse and Retrograde Degeneration of Retinal Ganglionic Cell

E. S. Guzman Barron, Chicago: On the Mechanism of Oxygen Poisoning

N. P. Arribas and T. F. Schlaegel, Jr., Indianapolis: Experimental Toxoplasmosis in the Rabbit

P. T. White and T. F. Schlaegel, Jr., Indianapolis: Results of Photic Driving on the Electroencephalograms of Patients with Suppression Amblyopia

N. Kent and T. F. Schlaegel, Jr., Indianapolis: Selective Perception in Hysterical Amblyopia

P. A. Cibis, M. Constant, and G. Pribyl, St. Louis: Effect of Beta-Hypophamine on Intraocular Pressure and Aqueous Flow in Human Eyes

M. A. Constant and B. Becker, St. Louis: Experimental Tonography. II. Effect of Various Compounds on the Intraocular Pressure of the Rabbit

R. D. Richards, Iowa City: Histologic Changes in Radiation Cataracts in Mice

M. Hobson Rice, Iowa City: Familial Occurrence of Developmental Anomalies of Cornea, Iris, and Chamber Angle with Visible Region of Schlemm's Canal

C. Matta, Iowa City: The Skin Test for Monoliasis

P. J. Hauser, Iowa City: Studies on the Fixation Pattern in Amblyopia ex Anopsia

F. C. Blodi, Iowa City: Influence of Newer Ganglioplegics on the Eye

M. Armaly, Iowa City: Comparison of Bulbar Pressure Test and Tonography

F. W. Newell and T. Sheftel, Chicago: Studies Concerning the Ocular Hypertensive Reaction Following Paracentesis

G. J. Wyman, Peoria, Ill.: Use of Versene in Removal of Rust in the Cornea

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FELLOWSHIPS IN OPHTHALMOLOGY

Eighteen fellowships for residents in ophthalmology will be established over the next three years by the Guild of Prescription Opticians of America, it has been announced by the Guild's President, Galen B. Kilburn, of Atlanta.

In announcing the adoption of the plan by the Guild's Board of directors, Mr. Kilburn said that its purpose is to encourage outstanding young physicians to become residents in ophthalmology by providing financial help during all three required years of residency.

Each fellowship will provide a total stipend of $1,800, payable in monthly instalments over the three-year period of residency. These fellowships are being provided on a regional basis, with the United States and Canada divided into six geographical areas, each having approximately the same number of three-year ophthalmology residencies available. Selection of the recipient in each area will be made by a Committee of Opthalmologists.

One fellowship in each of the six areas will be initiated this year, a second one next year, and a third one the third year, when the total number of fellowships will reach eighteen. Thereafter as each three-year residency is completed a new fellowship will become available, constantly maintaining the number of fellowships at eighteen.

Applications and information may be secured from the Guild of Prescription Opticians of America, Inc., 110 East 23rd Street, New York 10.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

The National Society for the Prevention of Blindness announces the availability of grants-in-aid for basic laboratory or clinical research projects that may add to the understanding of the etiology of blinding eye diseases or improve methods of diagnosis, treatment or prevention.

To be considered, applications should be received before April 1, 1956. Forms may be obtained from the Research Committee, National Society for the Prevention of Blindness, 1790 Broadway, New York 19, N. Y.

In December, the National Society reported new research grants totaling $12,200. These were allotted to the following persons for the projects indicated:

Dr. Gordon E. Gibbs, University of Nebraska Medical School, Omaha: Adrenocorticoid function in relation to diabetic retinitis.

Dr. Jerry H. Jacobson, New York Eye and Ear Infirmary: Electrophysiology of the eye.

Dr. Irving A. Leopold, Wills Eye Hospital, Philadelphia: Choroidal circulation.

Drs. A. Gerard DeVoe and Robert S. Coles, New York University Postgraduate Medical School: Use of pancreatic dornase in inflammatory ocular infections.

Dr. Daniel G. Vaughan, Jr., University of California School of Medicine, San Francisco: Evaluation of antibacterial agents against Pseudomonas aeruginosa.

Dr. Peter C. Kronfeld, Illinois Eye and Ear Infirmary, Chicago: Cardiovascular effects upon the human tonogram.

The 1956 "Sight-Saving Conference" of the National Society for the Prevention of Blindness will be held March 26-28 at the Palmer House in Chicago, Ill., it has been announced by the National Society for the Prevention of Blindness, conference sponsor.

Reports of new research into the causes of the blinding eye diseases will be made by outstanding ophthalmological investigators during the three-day sessions. Other highlights include the presentation of new techniques and procedures in various phases of sight conservation work in the fields of medicine, education, nursing, social work and safety. Many interesting related exhibits will be on display.

Several hundred delegates from all parts of the United States are expected at the three-day conference.

Individual reservations should be made directly with the Palmer House at Chicago. Advance programs may be obtained by writing to the National Society for the Prevention of Blindness, 1790 Broadway, New York 19.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

The Fortieth Annual Meeting of the Pacific Coast Oto-Ophthalmological Society will take place in Phoenix, Arizona, April 15-19, 1956.

Guest of Honor at the meeting is Horace G. Merrill, M.D., of San Diego, California, and the Guest Speaker is A. C. Furstenberg, M.D., dean of the Medical School and professor of otolaryngology, University of Michigan. There will be scientific and motion picture programs in otolaryngology and in ophthalmology throughout the week and instruction courses in both specialties on Tuesday.

President of the Society is Lester T. Jones, M.D., of Portland, Oregon, and John F. Tolan, M.D., of Seattle, is secretary-treasurer.

CALIFORNIA

The John MacKenzie Brown Memorial Fund has been established to perpetuate the name of the man who was known as the dean of otolaryngologists on the West Coast and who made contributions to the specialty which will be permanent in the archives of otolaryngology. This fund will be used to build a lecture hall in the new University of Southern California Medical School Center. This will be a fitting memorial to Doctor Brown, who was very eager to see education in medicine raised to the highest possible level.

Contributions to the U.S.C. Medical School, attention John Mackenzie Brown Memorial Fund, may be forwarded to the Fund office, Suite 308, 1136 West Sixth Street, Los Angeles 17.

COLORADO

A postgraduate course, "Ear, Nose and Throat Problems in General Practice," will be given at the University of Colorado Medical Center, Denver, March 15-17, with the cosponsorship of the Colorado Otolaryngological Society. The guest lecturer will be Dr. Francis L. Lederer, head, department of otolaryngology, University of Illinois College of Medicine, Chicago.

The course is open to all graduates of accredited medical schools and/or members of their respective medical societies. The registration fee will be $5 and tuition, $25. For application write to the Director of Postgraduate Medical Education, University of Colorado Medical Center, 4200 E. Ninth Ave., Denver 20.

GEORGIA

Dr. John R. Fair has been appointed assistant professor of surgery and chief of ophthalmology at the Medical College of Georgia, Augusta. Dr. Fair, who was formerly assistant director of the Ocular Research Unit, Walter Reed Army Medical Center, Washington, D. C., in 1954 served as chief of the eye section of the Army's 98th General Hospital in Germany, a post from which he resigned with the rank of Lieutenant Colonel.

ILLINOIS

The Chicago Ophthalmological Society held its clinical conference Feb. 10-11 at the Drake Hotel. A symposium on neu-

ro-ophthalmology included the following presentations by out-of-state speakers: "Oculomotor Nerve Palsies," C. Wilbur Rucker, Rochester, Minn.; "Clinical Applications of Electro-retinography," Hermann M. Burian, Iowa City; "A New Autonomic Drug," David A. Rosen, Kingston, Ont., Canada.

The Sanford R. Gifford Memorial Lecture, "Alterations in the Caliber of Retinal Vessels," was delivered by Dr. Rucker.

Saturday was devoted to a symposium on diabetic retinopathy in which Dr. Rosen's topic was "Experimental Diabetic Retinopathy" and Dr. Burian's was "Problems in the Diagnosis and Treatment of Strabismus." "New Approach for Scleral Shortening in Retinal Detachment" was presented by Dr. Ramon Castroviejo, New York.

Dr. Derrick Vail, professor and chairman of ophthalmology at Northwestern University Medical School, left Chicago on February 6 for a 30-day tour of the U. S. Army hospitals in the European Command. Dr. Vail will serve as a consultant in ophthalmology at the special request of the Surgeon General of the U. S. Army.

On the tour he will visit 15 Army hospitals in Berlin, Heidelberg, Munich, Frankfort, Paris and other European cities. The tour is part of the overseas consultant program in which well-known specialists visit Europe and the Far East.

Dr. Vail will give a series of lectures to medical officers in the hosptials and will participate in informal discussions, conferences, ward rounds and examination of patients. He will be a guest lecturer at the annual medical-surgical conference of all medical officers in the European Command held in Frankfort, Germany, Feb. 17-18.

Dr. Vail was recently elected second vice-president of the American College of Surgeons and was appointed to the council of the National Institute of Neurologic Diseases and Blindness of the U. S. Public Health Service. He is an honorary fellow of the Royal College of Surgeons of England and an honorary member of the Ophthalmological Society of the United Kingdom. He is director of the eye department at Passavant Memorial hospital.

A past president of the American Academy of Ophthalmology and Otolaryngology and of the Chicago Ophthalmology Society, Dr. Vail has also served on editorial boards of the American Journal of Ophthalmology, Quarterly Review of Ophthalmology, Excerpta Medica, Postgraduate Medicine and Year Book of Ophthalmology. A colonel in the Medical Corps, he received such honors as the Legion of Merit, Bronze Star, French Medal of Gratitude, and Order of the Crown of Belgium.

Northwestern University has announced the receipt of a gift of $7,000 from S. F. Posen, president of Beltone Hearing Aid Company, Chicago. The fund will be used for a new soundproof hearing laboratory which will make possible the conduct of research on various tests for the diagnosis of hearing impairments.

The soundproof testing chamber, with its control room and acoustical equipment, is being constructed in the department of otolaryngology in the Montgomery Ward Memorial building at the Northwestern University Medical Center on the Chicago campus of the University.

MICHIGAN

The department of postgraduate medicine at the University of Michigan Medical School, Ann Arbor, will hold an otolaryngology conference at the University Hospital, April 19-21, 1956, under the direction of Dr. Albert C. Furstenberg, chairman, Department of Otolaryngology. Guest lecturers, together with members of the staff of the Department of Otolaryngology, will participate in the program. For information, write to Dr. John M. Sheldon, Director, Department of Postgraduate Medicine, University Hospital, Ann Arbor.

MISSOURI

The St. Louis Ophthalmological Society met with the St. Louis Society for the Blind, January 26, 1956, for the presentation of the Leslie Dana Gold Medal for the Prevention of Blindness to Mrs. Helenor Campbell Foerster. Mrs. Foerster was formerly chief of the Eye Registry, Armed Forces Institute of Pathology, Washington, D. C.

At the scientific session Mrs. Foerster addressed the combined societies on the subject: "The Etiologic Factors in Intra-Ocular Granuloma."

The Gold Medal takes its name from the late Leslie Dana, former president of the St. Louis Society for the Blind. It is awarded annually by the St. Louis Society to a person selected by the National Society for the Prevention of Blindness.

Mrs. Foerster, the former Helenor Campbell Wilder, won the medal, the National Society announced, for accomplishments during her 30-year career with the Armed Forces Institute of Pathology in Washington, D. C. At her retirement in 1953, she was chief of its section on ophthalmic pathology.

While with the government in Washington, Mrs. Foerster completed studies in nematode ophthalmia and toxoplasmosis in ophthalmology. The disease of the eye demonstrated by Mrs. Foerster to be due to toxoplasma had puzzled pathologists for generations.

Mrs. Foerster was the first woman to be elected an honorary member of the American Academy of Ophthalmology and Otolaryngology and is the only person not possessing a medical degree to be elected a member of the American Association of Pathologists and Bacteriologists. In 1953, the Women's National Press Club in Washington designated her as "Woman of the Year in Science," and in 1954, when she retired from government service, she received the Exceptional Meritorious Award, highest civilian award in the Department of Defense.

NEBRASKA

Thursday, March 15, 1956, the Omaha Eye, Ear, Nose, and Throat Society and the Nebraska Academy of Ophthalmology and Otolaryngology are holding a joint all-day session. The principle speaker for ophthalmology will be Dr. Harold G. Scheie, of Philadelphia, and the principal speaker for otolaryngology will be Dr. George Shambaugh, Jr., of Chicago. Members of the neighboring ophthalmological and otolaryngological societies have been invited. The Kansas City Eye, Ear, Nose and Throat Society has made plans to attend as a group.

NEW YORK

Dr. Edwin B. Dunphy will deliver the annual Charles H. May Memorial Lecture, sponsored by the Eye Section of the New York Academy of Medicine, at the Academy on March 19, 1956. The subject will be "Radioactive Isotopes in Ophthalmology."

The Brooklyn Eye and Ear Hospital Alumni Association announces that its Fifth Annual Scientific Session will be held at the Brooklyn Eye and Ear Hospital on Saturday, April 7, 1956.

For Ophthalmology, the speakers and their titles will be as follows: Dr. Ralph I. Lloyd, "Glaucoma in 1900"; Dr. Willis S. Knighton, "Medical Treatment of Glaucoma"; Dr. Harold G. Scheie, "Surgical Management of Glaucoma"; Dr. Daniel Kravitz, "Gonioscopic Signincance in Glaucoma Surgery."

Motion pictures on the surgical treatment of glaucoma which will be shown are "Goniotomy and Goniopuncture in the Treatment of Congenital Glaucoma," by Dr. Harold G. Scheie; and "Cataract in Glaucoma," loaned through the courtesy of Dr. Wendell L. Hughes.

For Otolaryngology, the speakers and their titles will be the following: Dr. Philip Meltzer, "The Surgical Treatment of Deafness"; Dr. N. Lagoumis, "A Series of Case Reports of Peripheral Facial Nerve Paralysis"; Dr. Salmon Harvey, "Physical Aspects of Hearing and Equilibrium as Applied to the Human Ear"; Dr. L. A. Peer, "Plastic Surgery of Malformations of the External Ear"; and Dr. Irwin Fine, "DDx and Treatment of External Ear Disease."

OHIO

Ohio State University has announced its Postgraduate Course in Ophthalmology to be held at the Ohio State Union Building, March 5-6, 1956. Speakers will be Harold F. Falls, M.D., University of Michigan; Albert E. Sloane, M.D., Harvard University; Harvey Thorpe, M.D., University of Pittsburgh; and from Ohio State University, Gerhard Brecher, M.D., Robert H. Browning, M.D., William H. Havener, M.D., William Saunders, M.D., and Martin P. Sayers, M.D.

Registration fee is $20.00. Inquiries should be addressed to W. H. Havener, M.D., Department of Ophthalmology, University Hospital, Columbus, Ohio.

OREGON

The Oregon Academy of Ophthalmology and Otolaryngology and The University of Oregon Medical School, Portland, announces the Fifteenth Annual Spring Convention in Ophthalmology and Otolaryngology, March 19-22, 1956. There will be two separate programs. The ophthalmology lectures and demonstrations will be held all day Monday and Tuesday. The otolaryngology lectures and demonstrations will be held all day Wednesday and Thursday. Registration may be for one or both programs.

The fee for either one is $60.00; for both it is $90.00. Guest speakers will be Dr. Bernard Becker, professor of ophthalmology, Washington University Medical School, St. Louis; Dr. Samuel J. Kimura, assistant professor of ophthalmology, University of California Medical School, San Francisco; Dr. Frank D. Lathrop, associate otolaryngologist, Lahey Clinic, Boston; Dr. Howard P. House, professor and head of the department of otolaryngology, College of Medical Evangelists, Los Angeles.

To facilitate registration, the Committee would appreciate it if those planning to attend the courses would complete their reservations before registration day if possible.

The Secretary is Dr. Robert W. Zeller, 603 Mayer Building, Portland 5, Oregon.

TEXAS

Honor Guests at the Spring Clinical Conference of the Dallas Southern Clinical Society to be held March 12-14, 1956, include Dr. Franz Altmann, New York, and Dr. Paul J. Moses, San Francisco, for Otolaryngology; Dr. Trygve Gunderson, Boston, and Dr. Jack S. Guyton, Detroit, for Ophthalmology.

AUSTRIA

In its seminar congresses in ophthalmology the American Medical Society of Vienna, Austria, will present the following programs by the medical faculty of the University of Vienna:

Feb. 1-3, Tumors of the Eye; External Diseases of the Eye; Fundus Microscopy.

March 1-3, Anatomy of the Orbit and Adnexa; Indirect Ophthalmoscopy; Gross Pathology.

April 5-7, Histology of the Eye; Histopathology of the Eye; Ocular Muscle Anomalies.

May 3-5, Refraction, Ocular Motility; Perimetry.

June 7-9, Plastic Surgery of the Eye; External Diseases of the Eye; Glaucoma.

July 5-7, Slit Lamp Microscopy; Ophthalmoscopy; Ocular Therapeutics.

Aug. 2-4, Electrosurgical Treatment of the Eye; Ocular Cataracts; Retinal Detachment.

Sept. 6-8, Operative Ophthalmology; Gonioscopy; Anomalies.

Oct. 4-6, Neuro-ophthalmology; Diseases of the Retina; Physiology of the Eye.

Nov. 8-10, Ophthalmic Medicine; Diagnostic Examination; The Ocular Adnexa (Selected Topics).

Details may be obtained from the American Medical Society of Vienna, 1. Vienna, Universitaetsstrasse 11. Cable, "Ammedic," Vienna.

DENMARK

The First International Congress of Human Genetics will be held in Copenhagen, Denmark, August 1-6, 1956. This Congress is planned to cover all genetic aspects of normal and pathological characters in man. Any person interested in the subject of human genetics, especially medical genetics, is invited to take part in the Congress.

The provisional program and further information will be sent upon request. Write the Secretariate of the First International Congress of Human Genetics, The University Institute for Human Genetics, 14, Tagensveg, Copenhagen, N., Denmark.

IRELAND

The Irish Ophthalmological Society will hold its annual meeting in Dublin, May 10-12, 1956. The Montgomery Lecture will be delivered by Dr. Moacyr E. Alvaro, of Brazil, at 5 p.m. on Thursday, May 10, in Trinity College, Dublin.

POSITIONS AVAILABLE

There are vacancies for Resident Training in Otolaryngology to include bronchoesophagoscopy, rhinoplasty, allergy and surgery of otolaryngological cancer at the Veterans Administration Hospital, 130 West Kingsbridge Road, Bronx 68, New York. The residency is approved for three years and is supervised by consultants and attending physicians who are representatives of the Dean's Committee of the local medical schools. A basic science course is included in this training course and is conducted at Columbia University. Salary: $2640-$3300 per year.

For information write to Liaison Officer, Dean's Committee, Veterans Administration Hospital, 130 West Kingsbridge Road, Bronx 68, New York.

The Veterans Administration Hospital, Albuquerque, New Mexico, has an opening for an Ear, Nose, and Throat Specialist, with some ability in eye disease, to handle the in-patient references at the GM&S Hospital, 500 beds.

The hospital is affiliated with the University of Colorado Medical School for residency training in surgery, medicine, chest diseases, and pathology. The usual perquisites apply to anyone who is qualified, with a top salary of $13,760.00 to an individual who is board certified and of professorial rank.

Inquiries should be addressed to Lester J. Kantor, M.D., Director, Professional Services, Veterans Administration Hospital, Albuquerque, N.M.

The Sault Polyclinic, Sault Ste Marie, Michigan, has openings for eye, ear, nose and throat personnel. This is a ten-man modern clinic. Interested persons may write to H. M. Blair, M.D., at the above address.

Listings of positions available should be sent to W. L. Benedict, M.D., 100 First Avenue Building, Rochester, Minn., by the fifth of the month preceding publication. They should include (1) type of physician wanted (ophthalmologist or otolaryngologist; diplomate, resident, etc.); (2) type of position to be filled; and (3) whom to write for further information. Unless otherwise requested, listings will be published once only.

The Academy will handle no further correspondence beyond the listing and assume no responsibility. Neither does it endorse nor guarantee any of the published listings.

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